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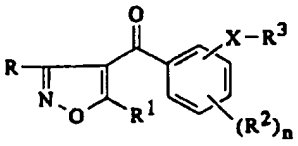
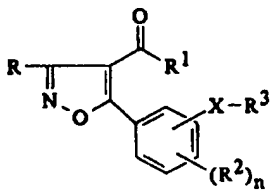
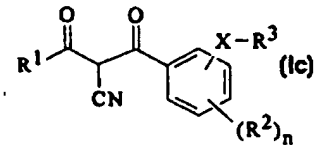

(Ia)


(Ib)


(Ic)

(57) Abstract

The invention relates to a 4-benzoylisoxazole derivative of formula (Ia), a 5-phenylisoxazole derivative of formula (Ib) or a 2-cyano-1,3-dione derivative of formula (Ic) wherein R^1, R^2, R^3, X and n are as defined in the description, and to their use as herbicides.

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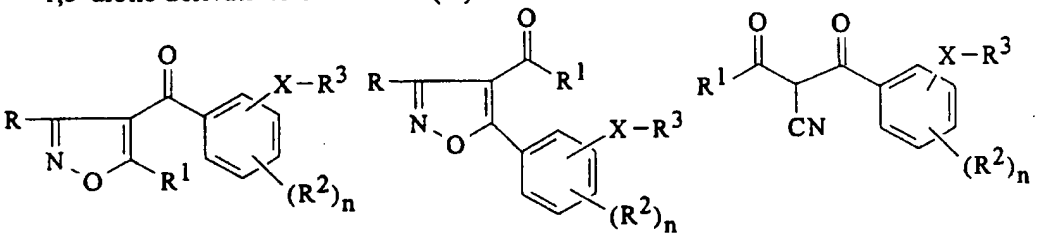
ISOXAZOLE AND 2-CYANO-1,3-DIONES DERIVATIVES AND THEIR USE AS HERBICIDES

This invention relates to novel 4-benzoylisoxazole derivatives, 5-phenylisoxazole derivatives, 2-cyano-1,3-dione derivatives, compositions containing them, processes for their preparation, intermediates in their preparation and their use as herbicides.

Herbicidal 4-benzoylisoxazoles are described in European Patent Publication Numbers 0418175, 0487357, 0527036, 0527037, 0560482 and 0560483. Herbicidal 2-cyano-1,3-diones are described in European Patent Publication Numbers 0213892, 0496630 and 0496631 and International Patent Publication No. WO 95/25099. Herbicidal 5-phenylisoxazoles are described in European Patent Publication Number 0524018. However none of the above publications disclose or suggest the presence of an aromatic heterocyclic ring linked by a ring nitrogen atom to a hydrocarbon group as a substituent on the phenyl ring.

The present invention provides 4-benzoylisoxazole derivatives of formula (Ia), 5-phenylisoxazole derivatives of formula (Ib) and 2-cyano-1,3-dione derivatives of formula (Ic):



(Ia) (Ib) (Ic)

wherein:

R represents hydrogen or $-CO_2R^4$;

R^1 represents:-

a straight- or branched- chain alkyl group containing up to six carbon atoms which is optionally substituted by one or more halogen atoms; or

a cycloalkyl group containing from three to six carbon atoms optionally substituted by one or more R^{12} groups or one or more halogen atoms;

R^2 represents:-

halogen;

a straight- or branched- chain alkyl group containing up to six carbon atoms which is substituted by one or more groups $-OR^5$;

a cycloalkyl group containing from three to six carbon atoms; or a group selected from nitro, cyano, $-CO_2R^5$, $-S(O)_pR^7$, $-O(CH_2)_mOR^5$, $-COR^5$, $-NR^5R^6$, $-N(R^8)SO_2R^7$, $-OR^7$, -OH, $-OSO_2R^7$, $-(CR^9R^{10})_tS(O)_qR^7$, $-CONR^5R^6$, $-N(R^8)-C(Z)=Y$, $-C(R^9R^{10})NR^8R^{11}$ and R^{12};

or two groups R^2, together with adjacent carbon atoms of the phenyl ring, form a 1,3-benzodioxole ring which is optionally substituted by one or two halogen (preferably chlorine or fluorine) atoms at the 2-position of the 1,3-benzodioxole ring;

n represents zero or an integer from one to three; where n is greater than one the groups R^2 may be the same or different;

m represents one, two or three;

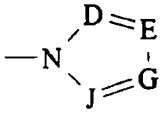
p represents zero, one or two;

q represents zero, one or two;

t represents one, two, three or four (preferably one);

X represents $-C(R^{13}R^{14})-$ or $-C(R^{13a}R^{14a})-C(R^{15}R^{16})-$;

R^3 represents a 5-membered heteroaromatic ring of formula (II)



(II)

in which D, E, G and J independently represent $-CR^{17}-$ or a nitrogen atom, with at least one of D, E, G and J representing $-CR^{17}-$;

two adjacent groups D, E, G and J may together form a second phenyl or 5- to 7- membered heteroaromatic ring optionally substituted by one or more groups R^{13b}, in which the 5- to 7- membered heterocyclic ring contains from one to four heteroatoms in the ring which may be the same or different selected from nitrogen, oxygen and sulphur;

R^4 represents:-

a straight- or branched- chain alkyl group containing up to six carbon atoms optionally substituted by one or more groups selected from halogen, $-OR^5$, $-CO_2R^5$, $-S(O)_pR^7$, phenyl and cyano;

or phenyl optionally substituted by one or more groups selected from halogen, $-OR^5$ and R^{12};

R^5 and R^6 which may be the same of different, each represents hydrogen or R^{12};

R^7 represents:-

R^{12}; or a cycloalkyl group containing from three to six carbon atoms; or a group $-(CH_2)_w$-[phenyl optionally substituted by from one to five groups R^{17a} which may be the same or different];

w represents zero or one;

R^8 represents:-

hydrogen;

a straight- or branched- chain alkyl, alkenyl or alkynyl group containing up to ten carbon atoms optionally substituted by one or more halogen atoms;

a cycloalkyl group containing from three to six carbon atoms;

$-(CH_2)_w$-[phenyl optionally substituted by from one to five groups R^{17a} which may be the same or different];

or $-OR^{18}$;

R^9 and R^{10} independently represent hydrogen or a straight- or branched- chain alkyl group containing up to six (preferably up to three) carbon atoms optionally substituted by one or more halogen atoms;

R^{11} represents $-S(O)_qR^7$ or $-C(Z)=Y$;

R^{12} represents:-

a straight- or branched- chain alkyl, alkenyl or alkynyl group containing up to six carbon atoms optionally substituted by one or more halogen atoms;

R^{13}, R^{13a}, R^{14a} and R^{15} independently represent R^5;

R^{13b} represents halogen, or R^{12};

R^{14} represents R^5, cyano, $-OR^{12}$, $-S(O)_pR^{12}$ or halogen;

R^{16} represents R^5, cyano, $-OR^{12}$ or $-S(O)_pR^{12}$;

R^{17} represents:-

a group selected from hydrogen, halogen, R^{18}, nitro, cyano, $-CO_2R^5$, $-S(O)_pR^{18}$, $-OR^{18}$, $-NR^5R^6$ and cyclopropyl;

R^{17a} represents R^{17} with the exclusion of hydrogen and cyclopropyl;

R^{18} represents a straight- or branched- chain alkyl group containing up to six carbon atoms which is optionally substituted by one or more halogen atoms;

Y is oxygen or sulphur (preferably Y represents oxygen);

Z represents a group selected from R^{12}, $-NR^8R^{19}$, $-NR^8-NR^{19}R^{20}$, $-SR^7$ and $-OR^7$;

R^{19} and R^{20} independently represent R^8;

and agriculturally acceptable salts and metal complexes thereof, which possess valuable herbicidal properties.

Compounds of formula (Ic) may exist in enolic tautomeric forms that may give rise to geometric isomers around the enolic double bond. Furthermore in certain cases the substituents R, R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8, R^9, R^{10}, R^{11}, R^{12}, R^{13}, R^{13a}, R^{13b}, R^{14}, R^{14a}, R^{15}, R^{16}, R^{17}, R^{17a}, R^{18}, R^{19}, R^{20}, X and Z may contribute to optical isomerism and/or stereoisomerism. All such forms are embraced by the present invention.

In the description that follows, reference to compounds of formula (I) means reference to a compound of formula (Ia), (Ib), or (Ic). It will be also understood that when X represents $-C(R^{13a}R^{14a})-C(R^{15}R^{16})-$ it is attached to the phenyl ring by the $-C(R^{13a}R^{14a})$ linking carbon.

By the term "agriculturally acceptable salts" is meant salts the cations or anions of which are known and accepted in the art for the formation of salts for agricultural or horticultural use. Preferably the salts are water-soluble. Suitable salts with bases include alkali metal (eg. sodium and potassium), alkaline earth metal (eg. calcium and magnesium), ammonium and amine (eg. diethanolamine, triethanolamine, octylamine, morpholine and dioctylmethylamine) salts. Suitable acid addition salts, formed by compounds of formula (I) containing an amino group, include salts with inorganic acids, for example hydrochlorides, sulphates, phosphates and nitrates and salts with organic acids, for example acetic acid.

By the term "metal complexes" is meant compounds in which one or both of the oxygen atoms of the 1,3-dione of formula (Ic) act as chelating agents to a metal cation. Examples of such cations include zinc, manganese, cupric, cuprous, ferric, ferrous, titanium and aluminium.

The compounds of the invention, in certain aspects of their properties, for example their control of Echinochloa oryzicola and their selectivity in paddy rice, show advantageous properties over known compounds.

Compounds of formula (I) in which the various symbols are as hereinbefore defined and R^{17} is selected from hydrogen, halogen, R^{18}, nitro, cyano, $-CO_2R^5$, $S(O)_pR^{18}$, $-OR^{18}$ and $-NR^5R^6$ are preferred.

Compounds of formula (Ia) above are also preferred.

Compounds in which the 2-position of phenyl is substituted are also preferred.

Compounds in which the $-XR^3$ group is at the 2- or 3- position of phenyl are preferred; most preferably it is at the 2-position.

Compounds in which X represents $-CHR^{13}-$ are preferred, most preferably X represents $-CH_2-$.

Preferably R^3 represents an N-linked ring of formula (II) in which:-

(a) D is nitrogen and E, G and J represent $-CR^{17}-$ (i.e. a pyrazol-1-yl group);

(b) D, G and J are $-CR^{17}-$ and E is nitrogen (i.e. an imidazol-1-yl group);

(c) D and G are nitrogen and E and J are $-CR^{17}-$ (i.e. a 1,2,4-triazol-1-yl group); or

(d) D and E are nitrogen and G and J are $-CR^{17}-$ (i.e. a 1,2,3-triazol-1-yl group).

Most preferably R^3 is a ring of formula (II) in which D is nitrogen, E and J are $-CR^{17}-$ and G is nitrogen or CR^{17}.

In formula (I) above, preferably the 5- and 6- positions of phenyl are unsubstituted.

Preferably R^1 represents a straight- or branched- chain alkyl group containing up to three carbon atoms which is optionally substituted by one or more halogen atoms; or cyclopropyl or 1-methylcyclopropyl.

Most preferably R^1 represents a cyclopropyl group.

Preferably R^2 represents halogen; a straight- or branched- chain alkyl or alkenyl group containing up to four carbon atoms optionally substituted by one or more halogen atoms; or a group selected from nitro, cyano, $-S(O)_pR^7$, $-OR^7$ and -OH.

Preferably n represents zero, one or two.

Preferably R^7 represents a straight- or branched- chain alkyl group containing up to six carbon atoms which is optionally substituted by one or more halogen atoms.

A preferred class of compounds of formula (Ia) above are those wherein:-

R represents hydrogen or $-CO_2R^4$;

R^1 represents cyclopropyl or 1-methylcyclopropyl;

R^2 represents:-

a straight- or branched- chain alkyl or alkenyl group containing up to three carbon atoms optionally substituted by one or more halogen atoms;

a group selected from halogen, nitro, cyano, $-S(O)_pR^7$, $-OR^7$ and -OH;

n represents zero, one or two;

X represents $-CHR^{13}-$;

R^3 represents an N-linked 5-membered heteroaromatic ring of formula (II) in which D, E, G and J independently represent $-CR^{17}-$ or a nitrogen atom, with at least one of D, E, G and J representing a CR^{17} group;

R^4 represents methyl or ethyl;

R^{13} represents hydrogen or a straight- or branched- chain alkyl or alkenyl group containing up to three carbon atoms optionally substituted by one or more halogen atoms.

A particularly preferred class of compounds of formula (Ia) above are those wherein:-

R represents hydrogen or $-CO_2R^4$;

R^1 represents cyclopropyl or 1-methylcyclopropyl;

R^2 represents:-

halogen; a straight- or branched- chain alkyl group containing up to three carbon atoms optionally substituted by one or more halogen atoms; or a group selected from $-S(O)_pR^7$ or $-OR^7$;

X represents $-CH_2-$;

R^3 represents a pyrazole, imidazole or 1,2,4-triazole ring;

R^4 represents a methyl or ethyl group;

R^7 represents:-

a methyl or ethyl group which is optionally substituted by one or more halogen atoms;

n represents 0, 1 or 2;

R^{17} represents hydrogen, methyl or ethyl.

A further particularly preferred class of compounds of formula (Ia) are those wherein:-

R represents hydrogen or $-CO_2R^4$;

R^1 represents cyclopropyl;

R^2 represents:-

halogen; a straight- or branched- chain alkyl group containing up to three carbon atoms optionally substituted by one or more halogen atoms; or $-S(O)_pR^7$;

X represents $-CH_2-$;

R^3 represents a pyrazole, imidazole or 1,2,4-triazole ring in which the ring carbon atoms bear a group R^{17};

R^4 represents a methyl or ethyl group;

R^7 represents a methyl or ethyl group which is optionally substituted by one or more halogen atoms;

n represents 0, 1 or 2; and

R^{17} represents hydrogen or a straight- or branched- chain alkyl group containing up to three carbon atoms.

A further particularly preferred class of compounds of formula (I) above are those wherein:-

R^1 represents cyclopropyl;

R^2 represents:-

halogen;

a straight- or branched- chain alkyl group containing up to three carbon atoms optionally substituted by one or more halogen atoms; or $-S(O)_pR^7$;

or two groups R^2, together with adjacent carbon atoms of the phenyl ring, form a 1,3-benzodioxole ring which is optionally substituted by one or two halogen (preferably chlorine or fluorine) atoms at the 2-position of the 1,3-benzodioxole ring;

X represents $-CH_2-$, -CH(Me)- or -CH(Et)-;

R^3 represents a pyrazole, imidazole or 1,2,4-triazole ring optionally substituted on the ring carbon atoms by one or two groups

selected from a straight- or branched- chain alkyl group containing up to four carbon atoms, $-S(O)_pR^{18}$ or cyclopropyl;

R^4 represents methyl or ethyl;

R^7 represents methyl or ethyl which are optionally substituted by one or more halogen atoms;

R^{18} is methyl or ethyl; and

n and p represent 0, 1 or 2.

The following compounds of formula (Ia) in which X is $-CH_2-$ and the group XR^3 is attached either to the 2-position of the phenyl ring (Table 1) or to the 3-position of the phenyl ring (Table 2) form part of the present invention. Note that in the Tables that follow, Me means methyl, Pr means propyl, cPr means cyclopropyl, 1-Me-cPr means 1-methylcyclopropyl and triazolyl refers to 1,2,4-triazolyl. Where subscripts do not appear in the Table it will be understood that in appropriate cases they are present (e.g. CO2CH3 means CO_2CH_3; CF3 means CF_3; 3,5-Me2-1-pyrazolyl means 3,5-dimethyl-1-pyrazolyl etc.)

Table 1

Cpd. No.	R	R^1	$(R^2)_n$	R^3
1	H	cPr	-	1-triazolyl
2	H	cPr	-	1-pyrazolyl
3	H	cPr	-	1-imidazolyl
4	H	cPr	-	3,5- Me2-1-pyrazolyl
5	H	cPr	-	3-Me-1-pyrazolyl
6	H	cPr	-	5-Me-1-pyrazolyl
7	H	cPr	-	2-Me-1-imidazolyl
8	H	cPr	-	4-Me-1-imidazolyl
9	H	cPr	-	5-Me-1-imidazolyl
10	H	1-Me-cPr	-	1-triazolyl
11	CO2CH3	cPr	-	1-triazolyl
12	CO2CH3	cPr	-	1-pyrazolyl
13	CO2CH3	cPr	-	1-imidazolyl
14	CO2C2H5	cPr	-	1-triazolyl
15	CO2C2H5	cPr	-	1-pyrazolyl
16	CO2C2H5	cPr	-	1-imidazolyl
17	H	cPr	4-CF3	1-triazolyl
18	H	cPr	4-CF3	1-pyrazolyl
19	H	cPr	4-CF3	3,5- Me2-1-pyrazolyl
20	H	cPr	4-CF3	3-Me-1-pyrazolyl
21	H	cPr	4-CF3	5-Me-1-pyrazolyl
22	H	1-Me-cPr	4-CF3	1-triazolyl
23	H	1-Me-cPr	4-CF3	1-pyrazolyl
24	CO2CH3	cPr	4-CF3	1-triazolyl
25	CO2CH3	cPr	4-CF3	1-pyrazolyl
26	CO2C2H5	cPr	4-CF3	1-triazolyl
27	CO2C2H5	cPr	4-CF3	1-pyrazolyl
28	H	cPr	4-Br	1-triazolyl
29	H	cPr	4-Br	1-pyrazolyl
30	H	cPr	4-Br	3,5- Me2-1-pyrazolyl
31	H	cPr	4-Br	3-Me-1-pyrazolyl
32	H	cPr	4-Br	5-Me-1-pyrazolyl
33	H	1-Me-cPr	4-Br	1-triazolyl
34	H	1-Me-cPr	4-Br	1-pyrazolyl
35	CO2CH3	cPr	4-Br	1-triazolyl
36	CO2CH3	cPr	4-Br	1-pyrazolyl
37	CO2C2H5	cPr	4-Br	1-triazolyl
38	CO2C2H5	cPr	4-Br	1-pyrazolyl

Cpd. No.	R	R^1	$(R^2)_n$	R^3
39	H	cPr	4-Br	1-triazolyl
40	H	cPr	4-Br	1-pyrazolyl
41	H	cPr	4-Br	3,5- Me2-1-pyrazolyl
42	H	cPr	4-Br	3-Me-1-pyrazolyl
43	H	cPr	4-Br	5-Me-1-pyrazolyl
44	H	1-Me-cPr	4-Br	1-triazolyl
45	H	1-Me-cPr	4-Br	1-pyrazolyl
46	CO2CH3	cPr	4-Br	1-triazolyl
47	CO2CH3	cPr	4-Br	1-pyrazolyl
48	CO2C2H5	cPr	4-Br	1-triazolyl
49	CO2C2H5	cPr	4-Br	1-pyrazolyl
50	H	cPr	4-Cl	1-triazolyl
51	H	cPr	4-Cl	1-pyrazolyl
52	H	cPr	4-Cl	3,5- Me2-1-pyrazolyl
53	H	cPr	4-Cl	3-Me-1-pyrazolyl
54	H	cPr	4-Cl	5-Me-1-pyrazolyl
55	H	1-Me-cPr	4-Cl	1-triazolyl
56	H	1-Me-cPr	4-Cl	1-pyrazolyl
57	CO2CH3	cPr	4-Cl	1-triazolyl
58	CO2CH3	cPr	4-Cl	1-pyrazolyl
59	CO2C2H5	cPr	4-Cl	1-triazolyl
60	CO2C2H5	cPr	4-Cl	1-pyrazolyl
61	H	cPr	4-F	1-triazolyl
62	H	cPr	4-F	1-pyrazolyl
63	H	cPr	4-F	3,5- Me2-1-pyrazolyl
64	H	cPr	4-F	3-Me-1-pyrazolyl
65	H	cPr	4-F	5-Me-1-pyrazolyl
66	H	1-Me-cPr	4-F	1-triazolyl
67	H	1-Me-cPr	4-F	1-pyrazolyl
68	CO2CH3	cPr	4-F	1-triazolyl
69	CO2CH3	cPr	4-F	1-pyrazolyl
70	CO2C2H5	cPr	4-F	1-triazolyl
71	CO2C2H5	cPr	4-F	1-pyrazolyl
72	H	cPr	4-SMe	1-triazolyl
73	H	cPr	4-SMe	1-pyrazolyl
74	H	cPr	4-SMe	3,5- Me2-1-pyrazolyl
75	H	cPr	4-SMe	3-Me-1-pyrazolyl
76	H	cPr	4-SMe	5-Me-1-pyrazolyl
77	H	1-Me-cPr	4-SMe	1-triazolyl

Cpd. No.	R	R^1	$(R^2)_n$	R^3
78	H	1-Me-cPr	4-SMe	1-pyrazolyl
79	CO2CH3	cPr	4-SMe	1-triazolyl
80	CO2CH3	cPr	4-SMe	1-pyrazolyl
81	CO2C2H5	cPr	4-SMe	1-triazolyl
82	CO2C2H5	cPr	4-SMe	1-pyrazolyl
83	H	cPr	3-Br	1-triazolyl
84	H	cPr	3-Br	1-pyrazolyl
85	H	cPr	3-Br	3,5- Me2-1-pyrazolyl
86	H	cPr	3-Br	3-Me-1-pyrazolyl
87	H	cPr	3-Br	5-Me-1-pyrazolyl
88	H	1-Me-cPr	3-Br	1-triazolyl
89	H	1-Me-cPr	3-Br	1-pyrazolyl
90	CO2CH3	cPr	3-Br	1-triazolyl
91	CO2CH3	cPr	3-Br	1-pyrazolyl
92	CO2C2H5	cPr	3-Br	1-triazolyl
93	CO2C2H5	cPr	3-Br	1-pyrazolyl
94	H	cPr	3-Cl	1-triazolyl
95	H	cPr	3-Cl	1-pyrazolyl
96	H	cPr	3-Cl	3,5- Me2-1-pyrazolyl
97	H	cPr	3-Cl	3-Me-1-pyrazolyl
98	H	cPr	3-Cl	5-Me-1-pyrazolyl
99	H	1-Me-cPr	3-Cl	1-triazolyl
100	H	1-Me-cPr	3-Cl	1-pyrazolyl
101	CO2CH3	cPr	3-Cl	1-triazolyl
102	CO2CH3	cPr	3-Cl	1-pyrazolyl
103	CO2C2H5	cPr	3-Cl	1-triazolyl
104	CO2C2H5	cPr	3-Cl	1-pyrazolyl
105	H	cPr	3-F	1-triazolyl
106	H	cPr	3-F	1-pyrazolyl
107	H	cPr	3-F	3,5- Me2-1-pyrazolyl
108	H	cPr	3-F	3-Me-1-pyrazolyl
109	H	cPr	3-F	5-Me-1-pyrazolyl
110	H	1-Me-cPr	3-F	1-triazolyl
111	H	1-Me-cPr	3-F	1-pyrazolyl
112	CO2CH3	cPr	3-F	1-triazolyl
113	CO2CH3	cPr	3-F	1-pyrazolyl
114	CO2C2H5	cPr	3-F	1-triazolyl
115	CO2C2H5	cPr	3-F	1-pyrazolyl
116	H	cPr	3-SMe	1-triazolyl

Cpd. No.	R	R^1	$(R^2)_n$	R^3
117	H	cPr	3-SMe	1-pyrazolyl
118	H	cPr	3-SMe	3,5- Me2-1-pyrazolyl
119	H	cPr	3-SMe	3-Me-1-pyrazolyl
120	H	cPr	3-SMe	5-Me-1-pyrazolyl
121	H	1-Me-cPr	3-SMe	1-triazolyl
122	H	1-Me-cPr	3-SMe	1-pyrazolyl
123	CO2CH3	cPr	3-SMe	1-triazolyl
124	CO2CH3	cPr	3-SMe	1-pyrazolyl
125	CO2C2H5	cPr	3-SMe	1-triazolyl
126	CO2C2H5	cPr	3-SMe	1-pyrazolyl
127	H	cPr	3,4-Cl2	1-triazolyl
128	H	cPr	3,4-Cl2	1-pyrazolyl
129	H	cPr	3,4-Cl2	3,5- Me2-1-pyrazolyl
130	H	cPr	3,4-Cl2	3-Me-1-pyrazolyl
131	H	cPr	3,4-Cl2	5-Me-1-pyrazolyl
132	H	1-Me-cPr	3,4-Cl2	1-triazolyl
133	H	1-Me-cPr	3,4-Cl2	1-pyrazolyl
134	CO2CH3	cPr	3,4-Cl2	1-triazolyl
135	CO2CH3	cPr	3,4-Cl2	1-pyrazolyl
136	CO2C2H5	cPr	3,4-Cl2	1-triazolyl
137	CO2C2H5	cPr	3,4-Cl2	1-pyrazolyl
138	H	cPr	4-OMe	1-triazolyl
139	H	cPr	4-OMe	1-pyrazolyl
140	CO2CH3	cPr	4-OMe	1-triazolyl
141	CO2CH3	cPr	4-OMe	1-pyrazolyl
142	CO2C2H5	cPr	4-OMe	1-triazolyl
143	CO2C2H5	cPr	4-OMe	1-pyrazolyl
144	H	cPr	3-CF3	1-triazolyl
145	H	cPr	3-CF3	1-pyrazolyl
146	CO2CH3	cPr	3-CF3	1-triazolyl
147	CO2CH3	cPr	3-CF3	1-pyrazolyl
148	CO2C2H5	cPr	3-CF3	1-triazolyl
149	CO2C2H5	cPr	3-CF3	1-pyrazolyl
150	H	cPr	3,4-Br2	1-triazolyl
151	H	cPr	3,4-Br2	1-pyrazolyl
152	CO2CH3	cPr	3,4-Br2	1-triazolyl
153	CO2CH3	cPr	3,4-Br2	1-pyrazolyl
154	CO2C2H5	cPr	3,4-Br2	1-triazolyl

Cpd. No.	R	R^1	$(R^2)_n$	R^3
155	CO2C2H5	cPr	3,4-Br2	1-pyrazolyl
156	H	cPr	3,4-F2	1-triazolyl
157	H	cPr	3,4-F2	1-pyrazolyl
158	CO2CH3	cPr	3,4-F2	1-triazolyl
159	CO2CH3	cPr	3,4-F2	1-pyrazolyl
160	CO2C2H5	cPr	3,4-F2	1-triazolyl
161	CO2C2H5	cPr	3,4-F2	1-pyrazolyl
162	H	cPr	3-Cl-4-CF3	1-triazolyl
163	H	cPr	3-Cl-4-CF3	1-pyrazolyl
164	CO2CH3	cPr	3-Cl-4-CF3	1-triazolyl
165	CO2CH3	cPr	3-Cl-4-CF3	1-pyrazolyl
166	CO2C2H5	cPr	3-Cl-4-CF3	1-triazolyl
167	CO2C2H5	cPr	3-Cl-4-CF3	1-pyrazolyl
168	H	cPr	3-Br-4-Cl	1-triazolyl
169	H	cPr	3-Br-4-Cl	1-pyrazolyl
170	CO2CH3	cPr	3-Br-4-Cl	1-triazolyl
171	CO2CH3	cPr	3-Br-4-Cl	1-pyrazolyl
172	CO2C2H5	cPr	3-Br-4-Cl	1-triazolyl
173	CO2C2H5	cPr	3-Br-4-Cl	1-pyrazolyl
174	H	cPr	3-Cl-4-Br	1-triazolyl
175	H	cPr	3-Cl-4-Br	1-pyrazolyl
176	CO2CH3	cPr	3-Cl-4-Br	1-triazolyl
177	CO2CH3	cPr	3-Cl-4-Br	1-pyrazolyl
178	CO2C2H5	cPr	3-Cl-4-Br	1-triazolyl
179	CO2C2H5	cPr	3-Cl-4-Br	1-pyrazolyl
180	H	cPr	3-F-4-Cl	1-triazolyl
181	H	cPr	3-F-4-Cl	1-pyrazolyl
182	CO2CH3	cPr	3-F-4-Cl	1-triazolyl
183	CO2CH3	cPr	3-F-4-Cl	1-pyrazolyl
184	CO2C2H5	cPr	3-F-4-Cl	1-triazolyl
185	CO2C2H5	cPr	3-F-4-Cl	1-pyrazolyl
186	H	cPr	3-SMe-4-Cl	1-triazolyl
187	H	cPr	3-SMe-4-Cl	1-pyrazolyl
188	CO2CH3	cPr	3-SMe-4-Cl	1-triazolyl
189	CO2CH3	cPr	3-SMe-4-Cl	1-pyrazolyl
190	CO2C2H5	cPr	3-SMe-4-Cl	1-triazolyl
191	CO2C2H5	cPr	3-SMe-4-Cl	1-pyrazolyl
192	H	cPr	3-F-4-SMe	1-triazolyl
193	H	cPr	3-F-4-SMe	1-pyrazolyl

Cpd. No.	R	R^1	$(R^2)_n$	R^3
194	CO2CH3	cPr	3-F-4-SMe	1-triazolyl
195	CO2CH3	cPr	3-F-4-SMe	1-pyrazolyl
196	CO2C2H5	cPr	3-F-4-SMe	1-triazolyl
197	CO2C2H5	cPr	3-F-4-SMe	1-pyrazolyl
198	H	cPr	4-SOMe	1-triazolyl
199	H	cPr	4-SOMe	1-pyrazolyl
200	H	cPr	4-SOMe	3,5- Me2-1-pyrazolyl
201	H	cPr	4-SOMe	3-Me-1-pyrazolyl
202	H	cPr	4-SOMe	5-Me-1-pyrazolyl
203	H	1-Me-cPr	4-SOMe	1-triazolyl
204	H	1-Me-cPr	4-SOMe	1-pyrazolyl
205	CO2CH3	cPr	4-SOMe	1-triazolyl
206	CO2CH3	cPr	4-SOMe	1-pyrazolyl
207	CO2C2H5	cPr	4-SOMe	1-triazolyl
208	CO2C2H5	cPr	4-SOMe	1-pyrazolyl
209	H	cPr	4-SO2Me	1-triazolyl
210	H	cPr	4-SO2Me	1-pyrazolyl
211	H	cPr	4-SO2Me	3,5- Me2-1-pyrazolyl
212	H	cPr	4-SO2Me	3-Me-1-pyrazolyl
213	H	cPr	4-SO2Me	5-Me-1-pyrazolyl
214	H	1-Me-cPr	4-SO2Me	1-triazolyl
215	H	1-Me-cPr	4-SO2Me	1-pyrazolyl
216	CO2CH3	cPr	4-SO2Me	1-triazolyl
217	CO2CH3	cPr	4-SO2Me	1-pyrazolyl
218	CO2C2H5	cPr	4-SO2Me	1-triazolyl
219	CO2C2H5	cPr	4-SO2Me	1-pyrazolyl

Table 2

Cpd. No.	R	R^1	$(R^2)_n$	R^3
251	H	cPr	-	1-triazolyl
252	H	cPr	-	1-pyrazolyl
253	H	cPr	-	3,5- Me2-1-pyrazolyl
254	H	cPr	-	3-Me-1-pyrazolyl
255	H	cPr	-	5-Me-1-pyrazolyl
256	H	1-Me-cPr	-	1-triazolyl
257	H	1-Me-cPr	-	1-pyrazolyl
258	CO2CH3	cPr	-	1-triazolyl
259	CO2CH3	cPr	-	1-pyrazolyl
260	CO2C2H5	cPr	-	1-triazolyl
261	CO2C2H5	cPr	-	1-pyrazolyl
262	H	cPr	2,4-Cl2	1-triazolyl
263	H	cPr	2,4-Cl2	1-pyrazolyl
264	H	1-Me-cPr	2,4-Cl2	1-triazolyl
265	H	1-Me-cPr	2,4-Cl2	1-pyrazolyl
266	CO2CH3	cPr	2,4-Cl2	1-triazolyl
267	CO2CH3	cPr	2,4-Cl2	1-pyrazolyl
268	CO2C2H5	cPr	2,4-Cl2	1-triazolyl
269	CO2C2H5	cPr	2,4-Cl2	1-pyrazolyl
270	H	cPr	2,4-Br2	1-triazolyl
271	H	cPr	2,4-Br2	1-pyrazolyl
272	H	1-Me-cPr	2,4-Br2	1-triazolyl
273	H	1-Me-cPr	2,4-Br2	1-pyrazolyl
274	CO2CH3	cPr	2,4-Br2	1-triazolyl
275	CO2CH3	cPr	2,4-Br2	1-pyrazolyl
276	CO2C2H5	cPr	2,4-Br2	1-triazolyl
277	CO2C2H5	cPr	2,4-Br2	1-pyrazolyl
278	H	cPr	2-Cl-4-F	1-triazolyl
279	H	cPr	2-Cl-4-F	1-pyrazolyl
280	H	1-Me-cPr	2-Cl-4-F	1-triazolyl
281	H	1-Me-cPr	2-Cl-4-F	1-pyrazolyl
282	CO2CH3	cPr	2-Cl-4-F	1-triazolyl
283	CO2CH3	cPr	2-Cl-4-F	1-pyrazolyl
284	CO2C2H5	cPr	2-Cl-4-F	1-triazolyl
285	CO2C2H5	cPr	2-Cl-4-F	1-pyrazolyl
286	H	cPr	2-F-4-Cl	1-triazolyl
287	H	cPr	2-F-4-Cl	1-pyrazolyl
288	H	1-Me-cPr	2-F-4-Cl	1-triazolyl

Cpd. No.	R	R^1	$(R^2)_n$	R^3
289	H	1-Me-cPr	2-F-4-Cl	1-pyrazolyl
290	CO2CH3	cPr	2-F-4-Cl	1-triazolyl
291	CO2CH3	cPr	2-F-4-Cl	1-pyrazolyl
292	CO2C2H5	cPr	2-F-4-Cl	1-triazolyl
293	CO2C2H5	cPr	2-F-4-Cl	1-pyrazolyl
294	H	cPr	2-Cl-4-SMe	1-triazolyl
295	H	cPr	2-Cl-4-SMe	1-pyrazolyl
296	H	1-Me-cPr	2-Cl-4-SMe	1-triazolyl
297	H	1-Me-cPr	2-Cl-4-SMe	1-pyrazolyl
298	CO2CH3	cPr	2-Cl-4-SMe	1-triazolyl
299	CO2CH3	cPr	2-Cl-4-SMe	1-pyrazolyl
300	CO2C2H5	cPr	2-Cl-4-SMe	1-triazolyl
301	CO2C2H5	cPr	2-Cl-4-SMe	1-pyrazolyl
302	H	cPr	2-Cl-4-SO2Me	1-triazolyl
303	H	cPr	2-Cl-4-SO2Me	1-pyrazolyl
304	H	1-Me-cPr	2-Cl-4-SO2Me	1-triazolyl
305	H	1-Me-cPr	2-Cl-4-SO2Me	1-pyrazolyl
306	CO2CH3	cPr	2-Cl-4-SO2Me	1-triazolyl
307	CO2CH3	cPr	2-Cl-4-SO2Me	1-pyrazolyl
308	CO2C2H5	cPr	2-Cl-4-SO2Me	1-triazolyl
309	CO2C2H5	cPr	2-Cl-4-SO2Me	1-pyrazolyl
310	H	cPr	2-Cl-4-SOMe	1-triazolyl
311	H	cPr	2-Cl-4-SOMe	1-pyrazolyl
312	H	1-Me-cPr	2-Cl-4-SOMe	1-triazolyl
313	H	1-Me-cPr	2-Cl-4-SOMe	1-pyrazolyl
314	CO2CH3	cPr	2-Cl-4-SOMe	1-triazolyl
315	CO2CH3	cPr	2-Cl-4-SOMe	1-pyrazolyl
316	CO2C2H5	cPr	2-Cl-4-SOMe	1-triazolyl
317	CO2C2H5	cPr	2-Cl-4-SOMe	1-pyrazolyl
318	H	cPr	2-SMe-4-Cl	1-triazolyl
319	H	cPr	2-SMe-4-Cl	1-pyrazolyl
320	H	cPr	2-SOMe-4-Cl	1-triazolyl
321	H	cPr	2-SOMe-4-Cl	1-pyrazolyl
322	H	cPr	2-SO2Me-4-Cl	1-triazolyl
323	H	cPr	2-SO2Me-4-Cl	1-pyrazolyl
324	CO2C2H5	cPr	2-SMe-4-Cl	1-triazolyl
325	CO2C2H5	cPr	2-SMe-4-Cl	1-pyrazolyl

Particularly important compounds of formula (I) include the following:

ethyl 5-cyclopropyl-4-[2-(1,2,4-triazol-1-ylmethyl)-4-trifluoromethylbenzoyl]isoxazole-3-carboxylate;

ethyl 5-cyclopropyl-4-[2-(1-pyrazolylmethyl)-4-trifluoromethylbenzoyl]isoxazole-3-carboxylate;

ethyl 5-cyclopropyl-4-[2-(1-pyrazolylmethyl)benzoyl]isoxazole-3-carboxylate;

ethyl 5-cyclopropyl-4-[2-(1,2,4-triazol-1-ylmethyl)benzoyl]isoxazole-3-carboxylate;

ethyl 5-cyclopropyl-4-[2-(1-imidazolylmethyl)benzoyl]isoxazole-3-carboxylate;

ethyl 5-cyclopropyl-4-[4-methylthio-2-(1-pyrazolylmethyl)-benzoyl]isoxazole-3-carboxylate;

ethyl 4-[3,4-dichloro-2-(1,2,4-triazol-1-ylmethyl)benzoyl]-5-cyclopropylisoxazole-3-carboxylate;

ethyl 4-[4-bromo-2-(1,2,4-triazol-1-ylmethyl)benzoyl]-5-cyclopropylisoxazole-3-carboxylate;

5-cyclopropyl-4-[4-methylthio-2-(1-pyrazolylmethyl)-benzoyl]isoxazole;

5-cyclopropyl-4-[2-(3,5-dimethylpyrazol-1-ylmethyl)-4-(methylthio)benzoyl]isoxazole;

4-[3,4-dichloro-2-(1-pyrazolylmethyl)benzoyl]-5-cyclopropylisoxazole;

4-[3,4-dichloro-2-(1,2,4-triazol-1-ylmethyl)benzoyl]-5-cyclopropylisoxazole;

4-[4-bromo-2-(1-pyrazolylmethyl)benzoyl]-5-cyclopropylisoxazole;

4-[4-bromo-2-(1,2,4-triazol-1-ylmethyl)benzoyl]-5-cyclopropylisoxazole;

5-cyclopropyl-4-[2-(3-methylpyrazol-1-ylmethyl)-4-(methylthio)benzoyl]isoxazole;

5-cyclopropyl-4-[2-(5-methylpyrazol-1-ylmethyl)-4-(methylthio)benzoyl]isoxazole;

5-cyclopropyl-4-[4-methylsulphinyl-2-(1-pyrazolylmethyl)-benzoyl]isoxazole;

ethyl 5-cyclopropyl-4-[4-methylsulphonyl-2-(1-pyrazolylmethyl)benzoyl]isoxazole-3-carboxylate;

ethyl 5-cyclopropyl-4-[2-(3,5-dimethylpyrazol-1-ylmethyl)-4-(methylsulphinyl)benzoyl]isoxazole-3-carboxylate;

ethyl 5-cyclopropyl-4-[2-(3,5-dimethylpyrazol-1-ylmethyl)-4-(methylsulphonyl)benzoyl]isoxazole-3-carboxylate;

5-cyclopropyl-4-[4-methylsulphonyl-2-(1-pyrazolylmethyl)benzoyl]isoxazole;

ethyl 4-[4-bromo-2-(2-methylthio-1-imidazolylmethyl)benzoyl]-5-cyclopropylisoxazole-3-carboxylate;

ethyl 4-[4-bromo-2-(3-methylthio-1,2,4-triazol-1-ylmethyl)benzoyl]-5-cyclopropylisoxazole-3-carboxylate;

ethyl 5-cyclopropyl-4-[2-(2-methylthio-1-imidazolylmethyl)benzoyl]isoxazole-3-carboxylate;

ethyl 5-cyclopropyl-4-[2-(3-methylthio-1,2,4-triazol-1-ylmethyl)benzoyl]isoxazole-3-carboxylate;

4-[4-bromo-2-(3-*tert*-butyl-5-methylthio-1,2,4-triazol-1-ylmethyl)benzoyl]5-cyclopropylisoxazole;

4-[4-bromo-2-(5-cyclopropyl-3-methylthio-1,2,4-triazol-1-ylmethyl)benzoyl]5-cyclopropylisoxazole;

ethyl 5-cyclopropyl-4-[2-(3-methylthio-1,2,4-triazol-1-ylmethyl)-4-(trifluoromethyl)benzoyl]isoxazole-3-carboxylate;

5-cyclopropyl-4-[2-(3-methylthio-1,2,4-triazol-1-ylmethyl)benzoyl]isoxazole;

5-cyclopropyl-4-[2-(5-methylthio-1,2,4-triazol-1-ylmethyl)benzoyl]isoxazole;

4-[4-bromo-2-(3-methylthio-1,2,4-triazol-1-ylmethyl)benzoyl]-5-cyclopropylisoxazole;

4-[4-bromo-2-(5-methylthio-1,2,4-triazol-1-ylmethyl)benzoyl]-5-cyclopropylisoxazole;

5-cyclopropyl-4-[3,4-dichloro-2-(3-methylthio-1,2,4-triazol-1-ylmethyl)benzoyl]isoxazole;

5-cyclopropyl-4-[3,4-dichloro-2-(5-methylthio-1,2,4-triazol-1-ylmethyl)benzoyl]isoxazole;

5-cyclopropyl-4-[2,4-dichloro-3-(1,2,4-triazol-1-ylmethyl)benzoyl]isoxazole;

5-cyclopropyl-4-[2,4-dichloro-3-(1-pyrazolylmethyl)benzoyl]isoxazole;

5-cyclopropyl-4-{2-[1-(1,2,4-triazol-1-yl)ethyl]benzoyl}isoxazole;

5-cyclopropyl-4-{4-fluoro-2-[1-(1,2,4-triazol-1-yl)ethyl]benzoyl}isoxazole;

5-cyclopropyl-4-{4-methylthio-2-[1-(1,2,4-triazol-1-yl)ethyl]benzoyl}isoxazole;

5-cyclopropyl-4-{2,2-difluoro-4-[1-(1,2,4-triazol-1-yl)ethyl]-1,3-benzodioxol-5-oyl}isoxazole;

4-{4-bromo-2-[1-(1,2,4-triazol-1-yl)propyl]benzoyl}-5-cyclopropylisoxazole;

5-cyclopropyl-4-{4-fluoro-2-[2-(1,2,4-triazol-1-yl)ethyl]benzoyl}isoxazole;

4-[4-bromo-2-(3-methylsulphinyl-1,2,4-triazol-1-ylmethyl)benzoyl]-5-cyclopropylisoxazole;

5-cyclopropyl-4-[3,4-dichloro-2-(3-methylsulphinyl-1,2,4-triazol-1-ylmethyl)benzoyl]isoxazole;

5-cyclopropyl-4-[3,4-dichloro-2-(5-methylsulphinyl-1,2,4-triazol-1-ylmethyl)benzoyl]isoxazole;

ethyl 5-cyclopropyl-4-[3,4-dichloro-2-(3-methylsulphinyl-1,2,4-triazol-1-ylmethyl)benzoyl]isoxazole-3-carboxylate;

ethyl 5-cyclopropyl-4-[3,4-dichloro-2-(5-methylsulphinyl-1,2,4-triazol-1-ylmethyl)benzoyl]isoxazole-3-carboxylate;

ethyl 4-[4-bromo-2-(3-*tert*-butyl-5-methylsulphinyl-1,2,4-triazol-1-ylmethyl)benzoyl]-5-cyclopropylisoxazole-3-carboxylate;

ethyl 4-[4-bromo-2-(5-cyclopropyl-3-methylsulphinyl-1,2,4-triazol-1-ylmethyl)benzoyl]-5-cyclopropylisoxazole-3-carboxylate;

5-cyclopropyl-4-{4-methylsulphinyl-2-[1-(1,2,4-triazol-1-yl)ethyl]benzoyl}isoxazole;

5-cyclopropyl-4-[2-(3-methylsulphonyl-1,2,4-triazol-1-ylmethyl)benzoyl]isoxazole;

4-[4-bromo-2-(3-methylsulphonyl-1,2,4-triazol-1-ylmethyl)benzoyl]-5-cyclopropylisoxazole;

5-cyclopropyl-4-[3,4-dichloro-2-(3-methylsulphonyl-1,2,4-triazol-1-ylmethyl)benzoyl]isoxazole;

5-cyclopropyl-4-[2-(5-methylsulphonyl-1,2,4-triazol-1-ylmethyl)benzoyl]isoxazole;

ethyl 5-cyclopropyl-4-[3,4-dichloro-2-(3-methylsulphonyl-1,2,4-triazol-1-ylmethyl)benzoyl]isoxazole-3-carboxylic acid;

ethyl 4-[4-bromo-2-(3-*tert*-butyl-5-methylsulphonyl-1,2,4-triazol-1-ylmethyl)benzoyl]-5-cyclopropylisoxazole-3-carboxylate;

ethyl 4-[4-bromo-2-(5-cyclopropyl-3-methylsulphonyl-1,2,4-triazol-1-ylmethyl)benzoyl]-5-cyclopropylisoxazole-3-carboxylate;

ethyl 5-cyclopropyl-4-[2-(3-methylsulphonyl-1,2,4-triazol-1-ylmethyl)-4-(trifluoromethyl)benzoyl]isoxazole-3-carboxylate;

ethyl 5-cyclopropyl-4-[2-(5-methylsulphonyl-1,2,4-triazol-1-ylmethyl)-4-(trifluoromethyl)benzoyl]isoxazole-3-carboxylate;

5-cyclopropyl-4-{4-methylsulphonyl-2-[1-(1,2,4-triazol-1-yl)ethyl]benzoyl}isoxazole;

ethyl 5-cyclopropyl-4-[3,4-dichloro-2-(3-methylthio-1,2,4-triazol-1-ylmethyl)benzoyl]isoxazole-3-carboxylate;

ethyl 4-[4-bromo-2-(5-methylthio-1,2,4-triazol-1-ylmethyl)benzoyl]-5-cyclopropylisoxazole-3-carboxylate;

ethyl 4-[4-bromo-2-(3-*tert*-butyl-5-methylthio-1,2,4-triazol-1-ylmethyl)benzoyl]-5-cyclopropylisoxazole-3-carboxylate;

ethyl 4-[4-bromo-2-(5-cyclopropyl-3-methylthio-1,2,4-triazol-1-ylmethyl)benzoyl]-5-cyclopropylisoxazole-3-carboxylate;

ethyl 4-[4-bromo-2-(3-cyclopropyl-5-methylthio-1,2,4-triazol-1-ylmethyl)benzoyl]-5-cyclopropylisoxazole-3-carboxylate;

ethyl 4-[4-bromo-2-(3-isopropyl-5-methylthio-1,2,4-triazol-1-ylmethyl)benzoyl]-5-cyclopropylisoxazole-3-carboxylate;

ethyl 4-[4-bromo-2-(5-isopropyl-3-methylthio-1,2,4-triazol-1-ylmethyl)benzoyl]-5-cyclopropylisoxazole-3-carboxylate;

4-{4-bromo-2-[1-(1,2,4-triazol-1-yl)ethyl]benzoyl}-5-cyclopropyl-isoxazole;

1-[4-bromo-2-(1-pyrazolylmethyl)]phenyl-2-cyano-3-cyclopropylpropan-1,3-dione; and

5-{4-bromo-2-[1-(1,2,4-triazol-1-yl)propyl]phenyl}-4-(cyclopropylcarbonyl)isoxazole .

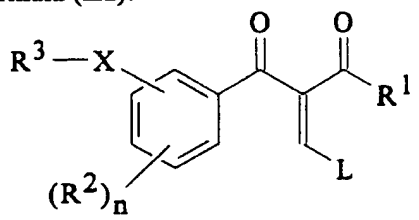
Compounds of formula (I) may be prepared by the application or adaptation of known methods (i.e. methods heretofore used or described in the literature), for example as hereinafter described.

In the following description where symbols appearing in formulae are not specifically defined, it is to be understood that they are "as hereinbefore defined" in accordance with the first definition of each symbol in the specification.

It is to be understood that in the descriptions of the following processes the sequences may be performed in different orders, and that suitable protecting groups may be required to achieve the compounds sought.

It is understood that when a process of the invention leads to the formation of a mixture of (Ia) and (Ib), these compounds may be separated by known methods.

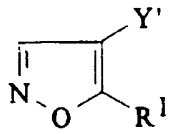
According to a feature of the present invention compounds of formula (Ia) or (Ib) in which R represents hydrogen and R^1, R^2, R^3, X and n are as defined above may be prepared by the reaction of a compound of formula (IIa):



(IIa)

wherein L is a leaving group and R^1, R^2, R^3, n and X are as hereinbefore defined, with hydroxylamine or a salt of hydroxylamine. Hydroxylamine hydrochloride is generally preferred. Generally L is alkoxy, for example ethoxy, or N,N-dialkylamino, for example dimethylamino. The reaction is generally carried out in an organic solvent such as ethanol or acetonitrile or a mixture of a water-miscible organic solvent and water, preferably in a ratio of organic solvent: water of from 1:99 to 99:1, optionally in the presence of a base or acid acceptor such as triethylamine or sodium acetate at a temperature from room temperature to the boiling point of the solvent. Compounds of formula (IIa) are novel and as such constitute a further feature of the present invention.

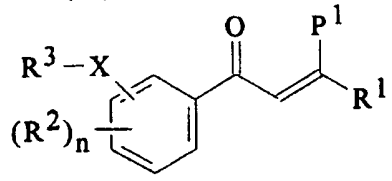
According to a further feature of the present invention compounds of formula (Ia) in which R represents hydrogen and R^1, R^2, R^3, X and n are as defined above may be prepared by the reaction of a compound of formula (III):



(III)

wherein R^1 is as hereinbefore defined and Y' represents a carboxy group or a reactive derivative thereof (such as a carboxylic acid chloride or carboxylic ester), or a cyano group, with an appropriate organometallic reagent such as a Grignard reagent or an organolithium reagent. The reaction is generally carried out in an inert solvent such as ether or tetrahydrofuran at a temperature from 0°C to the reflux temperature of the mixture.

According to a further feature of the present invention compounds of formula (Ia) wherein R represents a group $-CO_2R^4$ and R^1, R^2, R^3, X and n are as defined above, may be prepared by the reaction of a compound of formula (IV):

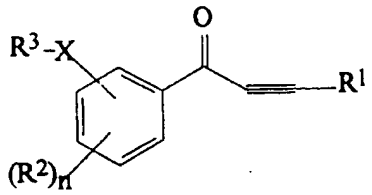


(IV)

wherein R^1, R^2, R^3, X and n are as hereinbefore defined and P^1 is a leaving group such as N,N-dialkylamino, with a compound of formula $R^4O_2CC(Z^1)$=NOH wherein R^4 is as hereinbefore defined and Z^1 is a halogen atom. Generally Z^1 is chlorine or bromine. The reaction is generally performed in an inert solvent such as toluene or dichloromethane either in the presence of a base such as triethylamine or a catalyst such as a 4 Angstrom molecular sieve or fluoride ion. Compounds of formula (IV) are novel and therefore constitute a further feature of the invention.

According to a further feature of the present invention compounds of formula (Ia) in which R represents a group $-CO_2R^4$ and R^1, R^2, R^3,

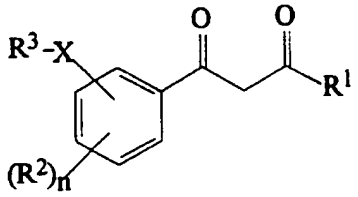
X and n are as defined above may be prepared by the reaction of a compound of formula (V):



(V)

wherein R^1, R^2, R^3, X and n are as hereinbefore defined, with a compound of formula $R^4O_2CC(Z^1)$=NOH wherein Z^1 and R^4 are as hereinbefore defined. The reaction is generally performed in an inert solvent such as toluene or dichloromethane optionally in the presence of a base such as triethylamine or a catalyst such as a 4 Angstrom molecular sieve or fluoride ion. The reaction is preferably carried out at a temperature between room temperature and the reflux temperature of the mixture. Compounds of formula (V) are novel and as such constitute a further feature of the present invention.

According to a further feature of the present invention compounds of formula (Ia) or (Ib) wherein R represents $-CO_2R^4$ and R^1, R^2, R^3, X and n are as defined above, may be prepared by the reaction of a salt of a compound of formula (VI):

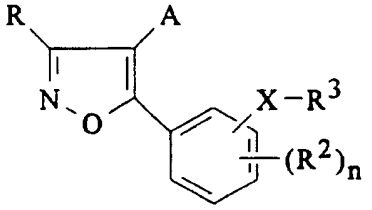


(VI)

wherein R^1, R^2, R^3, X and n are as hereinbefore defined with a compound of formula $R^4O_2CC(Z^1)$=NOH wherein R^4 and Z^1 are as hereinbefore defined. Preferred salts include sodium or magnesium salts. The reaction is generally performed in an inert solvent such as dichloromethane or acetonitrile at a temperature between room temperature and the reflux temperature of the mixture. The salt of a compound of formula (VI) is generally prepared in-situ by treating the compound of formula (VI) with a base. Examples of suitable bases

include alkaline earth metal alkoxides such as magnesium methoxide. Compounds of formula (VI) are novel and therefore constitite a further feature of the present invention.

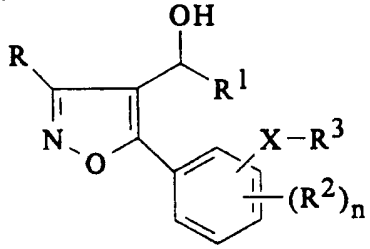
According to a feature of the present invention compounds of formula (Ib) in which R, R^1, R^2, R^3, X and n are as defined above, may be prepared by the metallation of a compound of general formula (VII):



(VII)

wherein R, R^2, X and n are as defined above and A is a halogen atom, followed by reaction of the compound thus obtained with an acid chloride of general formula R^1COCl wherein R is as defined above. Generally A is bromine or iodine and the reaction performed with for example n-butyllithium in an inert solvent such as ether or tetrahydrofuran at a temperature from -78°C to 0°C. Compounds of formula (VII) are novel and as such constitute a further feature of the invention.

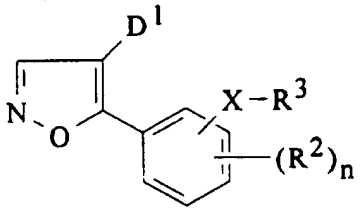
According to a further feature of the present invention compounds of formula (Ib) in which R, R^1, R^2, R^3, X and n are as defined above may be prepared by the oxidation of a compound of formula (VIII):



(VIII)

to convert the hydroxy group to a ketone group. The reaction is generally performed using an appropriate oxidising agent, for example, a mixture prepared from chromium trioxide and aqueous sulphuric acid. Compounds of formula (VIII) are novel and as such constitute a further feature of the invention.

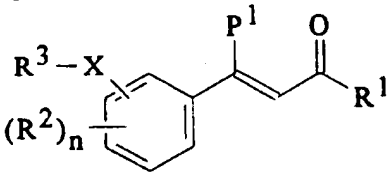
According to a further feature of the present invention compounds of general formula (Ib) in which R represents hydrogen and R^1, R^2, R^3, X and n are as defined above may be prepared by the reaction of a compound of formula (IX):



(IX)

in which D^1 represents a carboxy group, or a reactive derivative thereof (such as a carboxylic acid chloride or carboxylic ester), or a cyano group, with an appropriate organometallic reagent (for example Grignard or organolithium reagent), preferably of formula R^1M^1 in which M^1 is a metal halide such as magnesium bromide or a metal such as lithium. The reaction is generally carried out in an inert solvent such as ether or tetrahydrofuran, at a temperature from 0°C to the reflux temperature of the solvent. Compounds of formula (IX) are novel and therefore constitute a further feature of the invention.

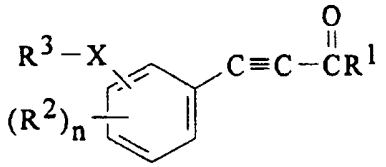
According to a further feature of the present invention compounds of general formula (Ib) in which R represents a $-CO_2R^4$ group and R^1, R^2, R^3, X and n are as defined above, may be prepared by the reaction of a compound of general formula (X):



(X)

wherein P^1 is as defined above, with a compound of general formula $R^4O_2CC(Z^1)$=NOH wherein Z^1 and R^4 are as hereinbefore defined. Generally Z^1 is chlorine or bromine. The reaction is preferably performed in an inert solvent such as toluene or dichloromethane either in the presence of a base such as triethylamine or a catalyst such as a 4 Angstrom molecular sieve or fluoride ion. Compounds of formula (X) are novel and therefore constitute a further feature of the invention.

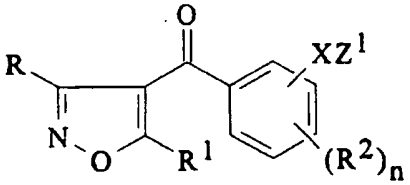
According to a further feature of the present invention compounds of general formula (Ib) in which R represents a group $-CO_2R^4$ and R^1, R^2, R^3, X and n are as defined above may be prepared by the reaction of a compound of general formula (XI):



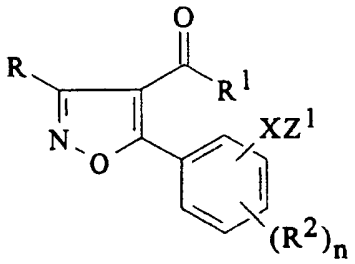
(XI)

with a compound of general formula $R^4O_2CC(Z^1)=NOH$ wherein Z^1 and R^4 are as hereinbefore defined. Generally Z^1 is chlorine or bromine. The reaction is preferably performed in an inert solvent such as toluene or dichloromethane, either in the presence of a base such as triethylamine, or a catalyst such as a 4 Angstrom molecular sieve or fluoride ion.

According to a further feature of the present invention compounds of formula (Ia) and (Ib) wherein R, R^1, R^2, R^3, R^4, X and n are as defined above, may be prepared by the reaction of a compound of formula (XII) and (XIII) respectively:



(XII)



(XIII)

wherein R, R^1, R^2, R^3, R^4 X, n and Z^1 are hereinbefore defined, with a compound of formula R^3-H. The reaction is generally performed in the presence of a base, for example sodium hydride or caesium carbonate, in an inert solvent, for example N,N-dimethylformamide at a temperature from 0°C to 100°C. The reaction is preferred where R represents $-CO_2R^4$.

According to a further feature of the present invention compounds of formula (Ia) and (Ib) wherein R, R^1, R^2, R^3, R^{13} and n are as defined above, X represents $-C(R^{13}R^{14})-$ and R^{14} represents a halogen atom,

may be prepared by the reaction of the corresponding compound of formula (Ia) or (Ib) wherein X represents -CHR^{13}- with a halogenating agent e.g. N-bromosuccinimide or N-chlorosuccinimide in an inert solvent, preferably carbon tetrachloride, in the presence of a radical initiator, e.g. benzoyl peroxide with irradiation by light from a Tungsten lamp at a temperature from ambient to the reflux temperature.

According to a further feature of the present invention compounds of formula (Ia) and (Ib) in which R, R^1, R^2, R^3 and n are as defined above, X represents -$C(R^{13a}R^{14a})$-$C(R^{15}R^{16})$- and R^{13a}, R^{14a}, R^{15} and R^{16} are as defined above may be prepared by the reaction of the corresponding compound of formula (XII) or (XIII) wherein X represents -$C(R^{13a})(R^{14a})$- and Z^1 is as defined above, preferably bromine or chlorine, with a compound of formula $HC(R^{15}R^{16})R^3$. The reaction is generally performed in the presence of a base e.g. sodium hydride and in an inert solvent e.g. N,N-dimethylformamide at a temperature from 0°C to 100°C.

According to a further feature of the present invention compounds of formula (Ia) or (Ib) in which R, R^1, R^2, R^3 and n are as defined above, and X represents -$C(R^{13})$(CN)- may be prepared by the reaction of the corresponding compound of formula (Ia) or (Ib) in which X is -$C(R^{13})$ (halogen)- with an alkali metal cyanide preferably sodium cyanide or potassium cyanide, in an inert solvent e.g. dimethylsulfoxide at a temperature from 10°C to 100°C. Preferably the halogen is bromine or chlorine.

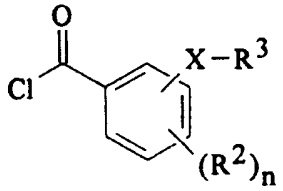
According to a further feature of the present invention compounds of formula (Ia) or (Ib) in which R, R^1, R^2, R^3, R^{12}, R^{13} and n are as defined above, and X represents -$C(R^{13})(OR^{12})$- may be prepared by the reaction of the corresponding compound of formula (Ia) or (Ib) in which X is -$C(R^{13})$(halogen)-, with a compound of formula $R^{12}OM$ where M represents hydrogen or an alkali metal (e.g. sodium, potassium or lithium). Preferably the halogen is bromine or chlorine. The reaction is generally performed in an inert solvent e.g. acetonitrile or N,N-dimethylformamide, optionally in the presence of a base e.g. sodium hydride, at a temperature from ambient to the reflux temperature.

According to a further feature of the present invention compounds of formula (Ia) or (Ib) in which R, R^1, R^2, R^3, R^{12}, R^{13} and n are as

defined above, and X represents -C(R^{13})(SR^{12})- may be prepared by the reaction of the corresponding compound of formula (Ia) or (Ib) wherein X is -C(R^{13})(halogen)-, by the same procedure as used for the compounds above wherein X represents -C(R^{13})(OR^{12})-, by replacing the compound $R^{12}OM$ by a compound $R^{12}SM$.

According to a feature of the present invention compounds of formula (Ic) may be prepared from the corresponding compound of formula (Ia) or (Ib) in which R is as defined above, or in which R is replaced by an amide or nitrile. Where R represents a hydrogen atom the reaction is preferably carried out by treatment with a base. Examples of suitable bases include alkali or alkaline earth metal hydroxides, alkoxides such as sodium ethoxide or organic bases such as triethylamine. Where R represents -CO_2R^4, or where R is replaced by amide or nitrile, the conversion is generally carried out by a hydrolytic reaction. The hydrolytic reaction may be performed in the presence of an acid or base. Acidic hydrolysis may be achieved for example using aqueous hydrochloric acid. Basic hydrolysis may be achieved for example using sodium hydroxide in a mixture of alcohol and water. The reactions are preferably carried out at a temperature between room temperature and the reflux temperature of the mixture. Compounds of formula (Ia) or (Ib) in which R is replaced by amide or nitrile are novel and thus constitute a further feature of the invention.

According to a further feature of the present invention, compounds of formula (Ic) in which R^1, R^2, R^3, X and n are as defined above may also be prepared by the reaction of a benzoyl chloride of formula (XIV):



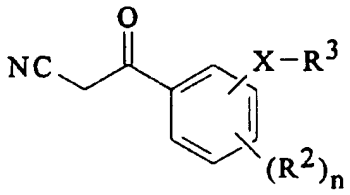
(XIV)

wherein R^2, R^3, X and n are as hereinbefore defined, with a beta-ketonitrile of formula (XV):

$R^1C(=O)CH_2CN$ (XV)

wherein R^1 is as hereinbefore defined. The reaction is generally performed in the presence of a base, in a solvent or solvent mixture. Suitable bases include metal hydrides, hydroxides or alkoxides (e.g. sodium or lithium hydride, sodium hydroxide, potassium hydroxide, magnesium ethoxide or magnesium methoxide). Suitable solvents include for example tetrahydrofuran; hydrocarbons such as toluene; or halogenated hydrocarbons such as dichloromethane. The reaction is generally performed at a temperature from 0°C to the reflux temperature. A number of compounds of formula (XIV) are novel and thus form a further feature of the invention.

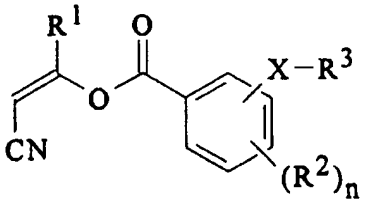
According to a further feature of the present invention, compounds of formula (Ic) in which R^1, R^2, R^3, X and n are as defined above may also be prepared by the reaction of an acid chloride of formula R^1COCl wherein R^1 is as hereinbefore defined, with a beta-ketonitrile of formula (XVI):



(XVI)

wherein R^2, R^3, X and n are as hereinbefore defined. The reaction is generally performed under the same conditions as described above for the reaction of compounds of formula (XIV) with compounds of formula (XV).

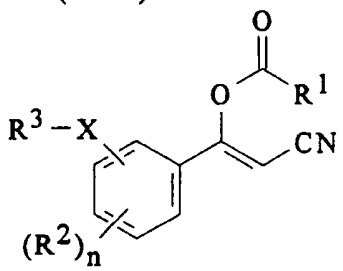
According to a further feature of the present invention compounds of formula (Ic) in which R^1, R^2, R^3, X and n are as defined above may also be prepared by the reaction of a benzoyl chloride of formula (XIV) above wherein R^2, R^3, X and n are as hereinbefore defined, with a beta-ketonitrile of formula (XV) wherein R^1 is as hereinbefore defined, via an intermediate of formula (XVII):



(XVII)

wherein R^1, R^2, R^3, X and n are as hereinbefore defined. The formation of the intermediate of formula (XVII) may be carried out in the presence of a mild base such as an organic base e.g. triethylamine, in an inert solvent such as acetonitrile or dichloromethane at a temperature between room temperature and the reflux temperature of the mixture. The rearrangement of the intermediate of formula (XVII) to a compound of formula (Ic) is generally carried out in situ in an inert solvent such as acetonitrile or dichloromethane in the presence of a catalyst such as a source of cyanide. Examples of such sources of cyanide are acetone cyanohydrin or an alkali metal cyanide such as potassium cyanide, optionally in the presence of a crown ether such as 18-crown-6.

According to a further feature of the present invention compounds of formula (Ic) in which R^1, R^2, R^3, X and n are as defined above, may be prepared by the reaction of an acid chloride of formula R^1COCl wherein R^1 is as hereinbefore defined, with a beta-ketonitrile of formula (XVI) wherein R^2, R^3, X and n are as hereinbefore defined via an intermediate of formula (XVIII):



(XVIII)

wherein R^1, R^2, R^3, X and n are as hereinbefore defined. The formation and rearrangement of the intermediate of formula (XVIII) is generally carried out under the same conditions as described above for the formation and rearrangement of compounds of formula (XVII).

Intermediates in the preparation of compounds of formula (Ia), (Ib) and (Ic) may be prepared by the application or adaptation of known methods.

Intermediates of formula (Ia) or (Ib) in which R is replaced by an amide or nitrile may be prepared by the reaction of a salt of a compound of formula (VI) with a compound of formula $P^2C(Z^1)$=NOH in which P^2 is amide or nitrile. The reaction is performed using the same conditions

as described for the preparation of compounds of formula (Ia) or (Ib) in which R is $-CO_2R^4$ from compounds of formula (VI).

Compounds of formula (IIa) may be prepared by the reaction of compounds of formula (VI) with either a trialkyl orthoformate such as triethyl orthoformate or a dimethylformamide dialkyl acetal such as dimethylformamide dimethyl acetal.

The reaction with a trialkyl orthoformate can be carried out in the presence of acetic anhydride at the reflux temperature of the mixture and the reaction with dialkylformamide dialkyl acetal is carried out optionally in the presence of an inert solvent at a temperature from room temperature to the reflux temperature of the mixture.

Compounds of formula (IV) may be prepared by the reaction of a compound of formula (XIX) with a benzoyl chloride of formula (XIV):

$$R^1C(P^1)=CH_2 \qquad (XIX)$$

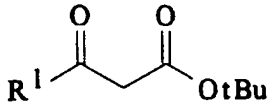
wherein R^1 and P^1 are as defined above. The reaction is generally carried out in the presence of an organic base such as triethylamine in an inert solvent such as toluene or dichloromethane at a temperature between -20°C and room temperature.

Compounds of formula (V) may be prepared by the metallation of the appropriate acetylene of formula (XX):

$$R^1C\equiv CH \qquad (XX)$$

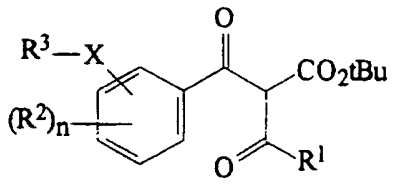
followed by reaction of the metal salt thus obtained with a benzoyl chloride of formula (XIV). The metallation is generally performed using n-butyl lithium in an inert solvent such as ether or tetrahydrofuran at a temperature from -78°C to 0°C. The subsequent reaction with the benzoyl chloride is carried out in the same solvent at a temperature between -78°C and room temperature.

Compounds of formula (VI) may be prepared by the reaction of an acid chloride of formula (XIV) with the metal salt of a compound of formula (XXI):



(XXI)

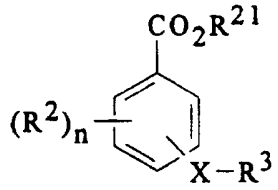
wherein R^1 is as hereinbefore defined, to give a compound of formula (XXII):



(XXII)

wherein R^1, R^2 R^3, X and n are as hereinbefore defined, which is subsequently decarboxylated to give a compound of formula (VI). Generally the reaction to produce the compound of formula (XXII) is performed in a solvent such as a lower alcohol, preferably methanol, in the presence of a metal, preferably magnesium. The reaction may also be performed using a pre-prepared metal salt of a compound of formula (XXI). The decarboxylation is generally performed by refluxing the compound of formula (XXII) in the presence of a catalyst, such as para-toluenesulphonic acid or trifluoroacetic acid, in an inert solvent e.g. toluene or 1,2-dichloroethane.

Compounds of formula (VI) may also be prepared by the reaction of a benzoic acid ester of formula (XXIII):



(XXIII)

wherein R^2, R^3, X and n are as hereinbefore defined and R^{21} represents a lower alkyl group, with a compound of formula (XXIV):

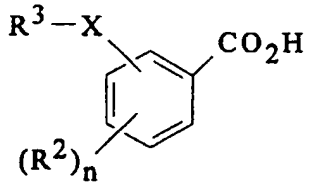
R^1-C(O)-CH_3 (XXIV)

wherein R^1 is as hereinbefore defined. The reaction is generally performed in a solvent such as ether, tetrahydrofuran or N,N-dimethylformamide, in the presence of a base, preferably an alkali metal base such as sodium hydride, at a temperature from 0°C to the reflux temperature. Compounds of formula (XXIII) are novel and as such constitute a further feature of the present invention.

Intermediates of formula (XII) or (XIII) may be prepared by any of the processes described above for the preparation of a compound of formula (Ia) or (Ib) from the corresponding compounds of formula (IIa), (III), (IV), (V), (VI), (VII), (VIII), (IX), (X) or (XI).

Intermediates of formula (XII) or (XIII) wherein X represents $-C(R^{13})(R^{14})-$ and R, R^1, R^2, R^{13}, R^{14}, Z^1 and n are defined above, may be prepared by the reaction of the corresponding compound of formula (XII) or (XIII) wherein Z^1 is replaced by a hydrogen atom, with a halogenating agent e.g. N-bromosuccinimide or N-chlorosuccinimide, in an inert solvent preferably carbon tetrachloride and in the presence of a radical initiator e.g. benzoyl peroxide, with irradiation by light from a tungsten lamp at a temperature from ambient to the reflux temperature.

Acid chlorides of formula (XIV) may be prepared by the reaction of a benzoic acid of formula (XXV):



(XXV)

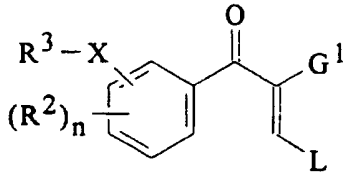
with a chlorinating agent, for example thionyl chloride at the reflux temperature of the mixture. In some cases the benzoyl chlorides may also be prepared by reaction of the benzoic acid with oxalyl chloride in a solvent such as 1,2-dichloroethane at from ambient to reflux temperature.

A number of the benzoic acids of formula (XXV) are novel and as such constitute a further feature of the present invention.

Esters of formula (XXIII) may be prepared from acids of formula (XXV) according to known methods.

Compounds of general formula (VIII) may be prepared by metallation of compounds of general formula (VII) wherein A represents bromine or iodine with for example n-butyllithium in an inert solvent such as ether or tetrahydrofuran at a temperature from -78°C to 0°C, followed by reaction with an aldehyde of general formula R^1CHO.

Compounds of general formula (IX) wherein D^1 is -CO_2-alkyl or -CN may be prepared by the reaction of compounds of general formula (XXVI):

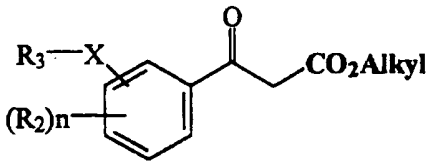


(XXVI)

wherein G^1 represents CO_2-alkyl or -CN and L is as hereinbefore defined, with a salt of hydroxylamine such as hydroxylamine hydrochloride, in a solvent such as ethanol or acetonitrile, optionally in the presence of a base or acid acceptor such as triethylamine or sodium acetate.

Compounds of general formula (IX) in which D^1 represents a carboxylic acid or carboxylic acid chloride may be prepared from the corresponding compound of general formula (IX) in which D^1 represents a carboxylic ester group by the hydrolysis of said ester group and conversion, as necessary, of the acid thus obtained to the acid chloride, e.g. by heating with thionyl chloride.

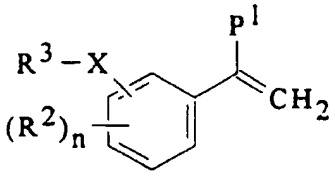
Compounds of general formula (XXVI) may be prepared by the reaction of a ketonitrile of formula (XVI) or a ketoester of formula (XXVII):



(XXVII)

with either triethyl orthoformate in the presence of acetic anhydride at the reflux temperature of the mixture or with dimethylformamide dimethylacetal optionally in an inert solvent such as toluene at a temperature from room temperature to the reflux temperature of the mixture.

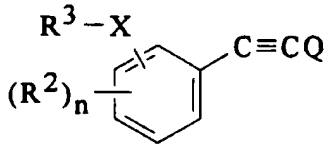
Compounds of general formula (X) may be prepared by the reaction of a compound of formula (XXVIII):



(XXVIII)

wherein P^1 is as hereinbefore defined, with an acid chloride of general formula R^1COCl in an inert solvent such as dichloromethane or toluene, in the presence of a base such as triethylamine.

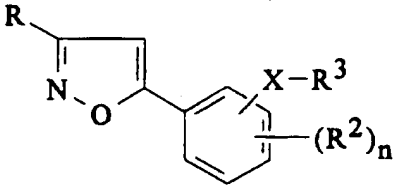
Compounds of general formula (XI) may be prepared by the metallation of the appropriate phenylacetylene of general formula (XXIX):



(XXIX)

wherein Q represents hydrogen or a bromine or iodine atom, using for example n-butyllithium in an inert solvent such as ether or tetrahydrofuran at a temperature from -78°C to 0°C, followed by treatment with an acid chloride of general formula R^1COCl.

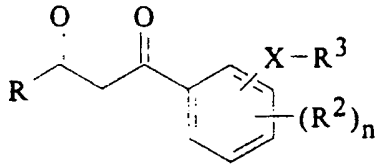
Compounds of general formula (VII) may be prepared by the halogenation of compounds of formula (XXX):



(XXX)

for example by heating with bromine or iodine in the presence of concentrated nitric acid. Compounds of formula (XXX) are novel and thus constitute a further feature of the invention.

Compounds of general formula (XXX) may be prepared by the reaction of compounds of formula (XXXI):



(XXXI)

with a salt of hydroxylamine such as hydrochloride, in a solvent such as ethanol or acetonitrile, optionally in the presence of a base or acid acceptor such as triethylamine or sodium acetate. Compounds of formula (XXXI) are novel and thus constitute a further feature of the invention.

Beta-ketonitriles of formula (XV) may be prepared from acid chlorides of formula R^1COCl by a number of methods well known in the chemical literature. For example, see Krauss, et al, Synthesis, **1983**, 308, or Muth, et al, J. Org. Chem, **1960**, 25, 736. Alternatively beta-ketonitriles of formula (XV) may be prepared by the reaction of an ester of formula R^1-CO_2Et, wherein R^1 is as hereinbefore defined, with acetonitrile. This reaction is described in the literature, for example see the article by Abramovitch and Hauser, J.Am. Chem. Soc., **1942**, 64, 2720.

Beta-ketonitriles of formula (XVI) may be prepared from benzoyl chlorides of formula (XIV) or from corresponding ethyl benzoates in a manner analogous to the preparation of beta-ketonitriles of formula (XV) set forth above.

Benzoic acids of formula (XXV) or esters of formula (XXIII) in which R^2, R^3, R^{21}, X and n are as defined above, may be prepared by the reaction of the corresponding compound of formula (XXV) or (XXIII) in which R^3 is replaced by a Z^1 (Z^1 preferably being bromine or chlorine), with a compound of formula R^3-H using the same procedure as described above for the preparation of compounds of formula (Ia) and (Ib) from compounds of formula (XII) and (XIII).

Intermediates of formula (III), (XIX), (XX), (XXI), (XXIV), (XXVII), (XXVIII), (XXIX) and (XXXI) are known or may be prepared by the application or adaptation of known methods.

Those skilled in the art will appreciate that some compounds of formula (I) may be prepared by the interconversion of other compounds

of formula (I) and such interconversions constitute yet more features of the present invention.

According to a further feature of the present invention compounds in which p and q is one or two may be prepared by the oxidation of the sulphur atom of the corresponding compounds in which p is 0 or 1. The oxidation of the sulphur atom is generally carried out using for example 3-chloroperoxybenzoic acid in an inert solvent such as dichloromethane at a temperature from -40°C to room temperature.

The following non-limiting Examples illustrate the preparation of compounds of formula (I) and the Reference Examples illustrate the preparation of intermediates in their synthesis. NMR Spectra are recorded as δ (ppm) in deuterochloroform as solvent for each of the compounds in these Examples and are listed in the following Table:-

TABLE 3

Comp. No.	1H-NMR
14	1.05-1.35(7H,m) 2.22(1H,m) 4.07(2H,q) 5.67(2H,s) 7.25-7.55(4H) 7.93(1H,s) 8.30(1H,s)
15	1.1-1.38(7H,m) 2.15(1H,m) 4.11(2H,q) 5.66(2H,s) 6.26(1H) 7.06(1H,d) 7.25-7.55(5H,m)
16	1.15(3H,t) 1.2(2H,m) 1.33(2H,m) 2.28(1H,m) 4.10(2H,q) 5.49(2H,s) 7.02(2H) 7.10(1H) 7.3-7.52(3H) 7.64(1H,s)
26	1.48(3H,t) 1.24(2H,m) 1.33(2H,m) 2.32(1H,m) 4.10(2H,q) 5.69(2H,s) 7.54(1H,d) 7.62(1H,s) 7.63(1H,d) 7.98(1H,s) 8.33(1H,s)
27	1.16(3H,t) 1.23(2H,m) 1.35(2H,m) 2.10(1H,m) 4.13(2h,q) 5.67(2H,s) 6.30(1H)7.32(1H) 7.6-7.65(4H)
28	1.24(2H,m) 1.37(2H,m) 5.54(2H,s) 7.40(1H,d) 7.52(1H,s) 7.61(1H,d) 7.90(1H,s) 8.20(1H,s) 8.25(1H,s)
29	1.22(2H,m) 1.33(2H,m) 2.53(1H,m) 5.50(2H,s) 6.22(1H) 7.3-7.4(3H)7.46-7.56(3H) 8.19(1H,s)
48	1.92(3H,t) 1.2(2H,m) 1.32(2H,m) 2.22(1H,m) 4.15(2H,q) 5.66(2H,s) 7.32(1H,d) 7.48(1H,d) 7.52(1H,d) 7.98(1H,dd) 8.34(1H)
73	1.20(2H,m) 1.32(2H,m) 2.43(3H,s) 2.55(1H,m) 5.67(2H,s) 6.24(1H) 6.88(1H)7.19(1H,dd) 7.42(1H,d) 7.48(2H) 8.22(1H,s)
74	1.18-1.23(2H,m) 1.34(2H,m) 2.17(6H) 2.61(1H,m) 5.42(2H,s) 5.81(1H,s) 6.58(1H,d) 7.16(1H,dd) 7.41(1H,d) 8.22(1H,s)
75,76	1.18-1.35(4H,m) 2.22(s) 2.38(s) 2.43(s) 2.54-2.63(1H,m) 5.46(s) 5.52(s) 5.98(d) 6.04(d) 6.55 6.89 7.17, 7.18, 7.35-7.43, 8.22, 8.26
82	1.12(3H,t) 1.17(2H,m) 1.28(2H,m) 2.23(1H,m) 2.48(3H,s) 4.06(2H,q) 5.53(2H,s) 6.28(1H) 7.15-7.7(3H) 7.48(1H) 7.52(1H)
127	1.25(2H,m) 1.35(2H,m) 2.53(1H,m) 5.73(1H,s) 7.32(1H,d) 7.60(1H,d) 7.78(1H,s) 8.17(2H)
128	1.18(2H,m) 1.29(2H,m) 2.48(1H,m) 5.70(2H,s) 6.00(1H) 7.24(1H,d) 7.30(1H) 7.52(1H) 7.53(1H,d) 8.12(1H,s)
136	1.18(2H,m) 1.25(3H,t) 1.32(2H,m) 2.17(1H,m) 4.20(2H,q) 5.82(2H,s) 7.38(1H,d) 7.58(1H,d) 7.86(1H,s) 8.20(1H,s)
199	1.24(2H,m) 1.35(2H,m) 2.59(1H,m) 2.75(3H,s) 5.56(2H,s) 6.21(1H) 7.37(1H) 7.45(1H) 7.48(1H) 7.63(1H,d) 7.75(1H,d) 8.17(1H,s)
200	1.25(3H,t) 1.23(2H,m) 1.35(2H,m) 2.08(3H,s) 2.19(3H,s) 2.63(1H,m) 2.74(3H,s) 5.37(2H) 5.74(1H,s) 7.18(1H,d) 7.62(1H,d) 7.74(1H,dd) 8.15(1H,s)
210	1.24(2H,m) 1.37(2H,m) 2.68(1H,m) 3.08(3H,s) 5.54(2H,s) 6.20(1H) 7.42(1H) 7.46(1H) 7.62(1H,d) 7.79(1H) 7.99(1H,dd) 8.11(1H)

Comp. No.	^{1}H-NMR
211	1.27(2H,m) 1.34(2H,m) 2.02(3H,s) 2.20(3H,s) 2.65(1H,m) 3.09(3H,s) 5.33(2H,s) 5.68(1H,s) 7.57(1H,d) 7.71(1H) 7.98(1H) 8.08(1H,s)
219	1.20(3H,t) 1.18-1.24(2H,m) 1.33(2H,m) 2.25(1H,m) 2.48(3H,s) 4.12(2H,q) 5.48(2H,s) 6.38(1H) 7.35-7.42(3H) 7.50(1H,s) 7.69(1H)
262	1.20-1.40(4H,m), 2.73(1H,m), 5.58(1H,s), 7.33(1H,d), 7.44(1H,d), 7.92(1H,s), 8.22(1H,s), 8.25(1H,s)
263	1.15-1.4(4H,m), 2.48(m), 2.73(m), 5.55(s), 5.68(s), 6.24(1H,m), 7.37.55(4H), 8.20(s), 8.25(s)
326	1.20-1.38(7H,m), 2.25(1H,m), 2.61(3H,s), 4.20(2H,q), 5.47(2H,s), 7.02(1H,d), 7.15(1H,s), 7.33(1H,d), 7.47(1H,dd)
327	1.84(3H,t), 1.18-1.46(4H,m), 2.18-2.25(1H,m), 2.59(3H.s), 4.15(2H,q) 5.57(2H,s), 7.42(1H,d), 7.50-7.54(2H,m), 8.23(1H,s)
328	1.13(3H,t), 1.15-1.35(4H,m), 2.25(1H,m),2.58(3H,s), 4.08(2H,m), 5.61(2H,s), 7.36-7.41(2H,m), 7.45-7.57(3H,m), 8.22(1H,s)
329	1.24(2H,m), 1.27(9H,s), 1.35(2H,m), 2.63(3H,s), 2.64(1H,m), 5.43(2H,s), 7.27(1H,d), 7.37(1H,d), 7.53(1H,dd), 8.23(1H,s)
330	1.05(4H,m), 1.25(2H,m), 1.37(2H,m), 1.80(1H,m), 2.44(3H,s), 2.59(1H,m), 5.53(2H,s), 7.37(1H,d), 7.38(1H,d), 7.57(1H,dd), 8.22(1H,s)
331	1.10-1.40(7H,m), 2.19-2.35(1H,m), 2.57(3H,s), 4.19(2H,q), 5.61(2H,s), 7.55(1H,d), 7.64(1H,d), 7.70(1H,s), 8.24(1H,s)
332	1.23(2H,m), 1.36(2H,m), 2.51(3H,s), 5.60(1H,m), 5.49(2H,s), 7.38-7.55(4H,m), 8.13(1H,s), 8.23(1H,s)
333	1.25(2H,m), 1.36(2H,m), 2.61(1H,m), 2.65(3H,s), 7.13(1H,d), 7.38-7.53(3H,m), 7.82(1H,s), 8.26(1H,s)
334	1.26(2H,m), 1.36(2H,m), 2.51(3H,s), 2.58(1H,m), 5.45(2H,s), 7.39(1H,d), 7.56(1H,d), 7.58(1H,dd), 8.14(1H,s), 8.20(1H,s)
335	1.26(2H,m), 1.35(2H,m), 2.64(1H,m), 2.67(3H,s), 5.46(2H,s), 7.30(1H,d), 7.39(1H,d), 7.57(1H,dd), 7.83(1H,s), 8.25(1H,s)
336	1.25(2H,m), 1.36(2H,m), 2.34(3H,s), 2.55(1H,m), 5.68(2H,s), 7.34(1H,d), 7.60(1H,d), 8.09(1H,s), 8.20(1H,s)
337	1.23(2H,m), 1.33(2H,m), 2.15(1H,m), 2.68(3H,s), 5.56(2H,s), 7.30(1H,d), 7.59(1H,d), 7.63(1H,s), 8.21(1H,s)
338	1.30(2H,m), 1.38(2H,m), 2.63(1H,m), 2.97(3H,t), 5.55(2H,q), 7.45(1H,d), 7.65(1H,dd), 7.70(1H,d), 8.21(1H,s), 8.46(1H,s)
339	1.27(2H,m), 1.39(2H,m), 2.64(1H,m), 2.89(3H,s), 5.77(2H,s), 7.41(1H,d), 7.66(1H,d), 8.22(1H,s), 8.31(1H,s)
340	1.25(2H,m), 1.37(2H,m), 2.63(1H,m), 6.02(1H,d), 6.15(1H,d), 7.37(1H,d), 7.63(1H,d), 7.78(1H,s), 8.22(1H,s)
341	1.02-1.04(7H,m), 2.20(1H,m), 2.98(3H,s), 4.20(2H,q), 5.85(2H,q), 7.27(1H,s), 7.38(1H,d), 7.59(1H,d), 8.33(1H,s)

Comp. No.	^{1}H-NMR
342	1.15(2H,m), 1.26(3H,t), 1.31(2H,m), 2.15(1H,m), 3.23(3H.s), 4.25(2H,q), 6.13(2H,q), 7.42(1H,d), 7.59(1H,d), 7.86(1H,s)
343	1.18(2H,m), 1.19(3H,t), 1.30(2H,m), 1.31(9H,s), 2.21(1H,m), 3.11(3H,s), 4.18(2H,q), 5.96(2H,q), 7.28(1H,d), 7.39(1H,d), 7.50(1H,dd)
344	1.08(2H,m), 1.20(2H,m), 1.23(3H,t), 1.25(2H,m), 1.35(2H,m), 1.98(1H,m), 2.25(1H,m), 2.98(3H,s), 4.17(2H,q), 5.80(2H,q), 7.16(1H,d), 7.36(1H,d), 7.51(1H,dd)
345	1.3(2H,m), 1.4(2H,m), 1.9(3H,d), 2.3(1H,m), 2.7(3H,s), 5.9(1H,m), 7.8(6H,m), 8.1(1H,s)
346	1.2-1.4(4H,m), 2.0(3H,d), 2.6(1H,m), 6.1(1H,m), 7.4-7.5(4H,m), 7.9(1H,s), 8.2(1H,s), 8.2(1H,s)
348	1.1(2H,m), 1.2(2H,m), 1.9(3H,d), 2.4(3H,s), 2.5(1H,m), 6.1(1H,q), 7.4(5H,m), 8.2(1H,s)
350	0.9(3H,t), 1.2-1.4(6H, m), 2.2-2.3(3H,m), 2.6(2H,m), 5.8(1H,m),7.4(1H,d), 7.6(1H,m), 7.9(1H,s), 8.0(1H, s), 8.2(1H,s), 8.5(1H,s)
351	1.2-1.4(4H,m), 2.6(2H, m), 3.3(2H,t), 4.6(2H, t), 6.8(1H, m), 7.0(1H, m), 7.5(1H, m), 8.0(2H, s), 8.2(1H,s)
352	1.29(2H,m), 1.40(2H,m), 2.67(1H,m), 3.22(3H,s), 5.59(2H,s), 7.50-7.60(4H,m), 8.25(1H,s), 8.51(1H,s)
353	1.25-1.40(4H,m), 3.21(3H,s), 5.57(2H,s), 7.47(1H,d), 7.67(1H,dd), 7.72(1H,d), 8.23(1H,s), 8.53(1H,s)
354	1.30(2H,m),1.40(2H,m),2.64(1H,m),3.15(3H,s), 5.78(2H,s), 7.43(1H,d), 7.68(1H,d), 8.22(1H,s), 8.32(1H,s)
355	1.25(2H,m), 1.38(2H,m), 2.64(1H,m), 3.45(3H,s), 6.09(2H,s), 7.39(1H,d), 7.65(1H,d), 7.79(1H,s), 8.23(1H,s)
356	1.21-1.40(7H,m), 2.38(1H,m), 3.23(3H,s), 4.19(2H,q), 5.88(2H,s), 7.37(1H,d), 7.60(1H,d), 8.33(1H,s)
357	1.16(2H,m), 1.20(3H,t), 1.31(2H,m), 1.33(9H,s), 2.15(1H,m), 3.37(3H,s), 4.20(2H,q), 6.00(2H,s), 7.21(1H,d), 7.42(1H,d), 7.50(1H,dd)
358	1.10(2H,m), 1.25(7H,m), 1.35(2H,m), 2.00(1H,m), 2.26(1H,m), 3.24(3H,s), 4.16(2H,q), 5.84(2H,s), 7.18(1H,d), 7.36(1H,d), 7.53(1H,dd)
359	1.16(3H,t), 1.25-1.43(4H,m), 2.33-2.45(1H,m), 3.25(3H,s), 4.10(2H,q), 5.74(2H,s), 7.58(1H,d), 7.69(1H,d), 7.83(1H,s), 8.55(1H,s)
360	1.13-1.43(7H,m), 2.10-2.25(1H,m), 3.42(3H,s), 4.17(2H,q), 6.10(2H,s), 7.49(1H,s), 7.67(2H,s), 7.99(1H,s)
361	1.2(4H,m), 1.9(3H,d), 2.5(1H,m), 3.0(3H,s), 6.0(1H,m), 8.0(5H,m), 8.3(1H,s)
362	1.18-1.35(7H,m), 2.15(1H,m), 2.49(3H,s), 4.22(2H,q), 5.75(2H,s), 7.37(1H,d), 7.57(1H,d), 8.09(1H,s)
363	1.12(3H,t), 1.15(2H,m), 1.39(2H,m), 4.07(2H,q), 4.33(2H,s), 5.61(2H,s), 7.22-7.55(9H,m), 8.23(1H,s)

Comp. No.	^{1}H-NMR
364	1.15-1.45(7H,m)1.34(9H,s), 2.20(1H,m), 2.86(3H,s), 4.17(2H,q), 5.60(2H,s), 7.00(1H,d), 7.38(1H,d), 7.48(1H,dd)
365	0.94-1.45(11H,m), 1.85(1H,m), 2.23(1H,m), 2.54(3H,s), 4.15(2H,q), 5.70(2H,s), 7.19(1H,d), 7.34(1H,d), 7.48(1H,dd)
366	0.94(4H,m), 1.20(2H,m), 1.21(3H,t), 1.33(2H,m), 2.00(1H,m), 2.15(1H,m), 2.64(3H,s), 4.20(2H,q), 5.53(2H,s), 7.12(1H,d), 7.39(1H,d), 7.50(1H,dd)
367	1.19(3H,t), 1.20(2H,m), 1.30(2H,m), 1.31(6H,d), 2.18(1H,m), 2.67(3H,s), 3.05(1H,m), 4.09(2H,q), 5.59(2H,s), 7.03(1H,d), 7.39(1H,d), 7.50(1H,dd)
368	1.20-1.35(4H,m),1.21(3H,t),1.28(6H,d), 2.24(1H,m), 2.58(3H,s), 3.06(1H,m), 4.18(2H,q), 5.62(2H.s), 7.08(1H,d), 7.34(1H,d), 7.47(1H,dd)
370	1.18-1.41(4H,m), 2.32-2.43(1H,m), 5.44(2H,s), 6.29(1H,t), 7.24(1H,d), 7.40-7.58 (4H,m)
371	0.9(2H,m), 1.2(2H,m), 1.3(3H,t), 1.9(1H,m), 2.2(1H, m), 2.4(1H,m), 5.3(1H,m), 7.3(1H,d), 7.6(1H,d), 7.9(1H,s), 8.1(1H,s), 8.3(1H,s), 8.8(1H,s)
372	1.16(3H,t), 1.15-1.25(2H,m), 1.30-1.37(2H,m), 2.21-2.30(1H,m), 2.59(3H,s), 4.13(2H,t), 5.50(2H,s), 6.90(1H,d), 7.04(1H,s), 7.13(1H,s), 7.33(1H,t), 7.45-7.52(2H,m)

Example 1

To a solution of ethyl 5-cyclopropyl-4-(2-methyl-4-trifluoromethylbenzoyl)isoxazole-3-carboxylate (0.81g) in carbon tetrachloride, N-bromosuccinimide (0.48g) and benzoylperoxide (0.01g) were added at room temperature. The reaction mixture was exposed to the light of an ordinary 300W light bulb placed 5-6 cm from the flask for 2 hours under reflux conditions. The reaction mixture was cooled to room temperature, succinimide removed by filtration and the filtrate concentrated under reduced pressure. N,N-Dimethylformamide was added to the residue and this solution added dropwise at room temperature to a solution of 1,2,4-triazole (0.23g) and sodium hydride (60% in mineral oil, 0.13g) in N,N-dimethylformamide. The reaction mixture was stirred at ambient temperature, water was added, and the mixture was extracted with ethyl acetate. The extract was washed with brine, dried over anhydrous $MgSO_4$, and evaporated. Purification by silica gel flash chromatography (n-hexane/ethyl acetate) gave ethyl 5-cyclopropyl-4-[2-(1,2,4-triazol-1-ylmethyl)-4-trifluoromethylbenzoyl] isoxazole-3-carboxylate (Compound 26, 0.35g).

The following compounds were prepared in a similar manner:

ethyl 5-cyclopropyl-4-[2-(1-pyrazolylmethyl)-4-trifluoromethylbenzoyl]isoxazole-3-carboxylate (Compound 27),

ethyl 5-cyclopropyl-4-[2-(1-pyrazolylmethyl)benzoyl]isoxazole-3-carboxylate (Compound 15),

ethyl 5-cyclopropyl-4-[2-(1,2,4-triazol-1-ylmethyl)benzoyl]isoxazole-3-carboxylate (Compound 14),

ethyl 5-cyclopropyl-4-[2-(1-imidazolylmethyl)benzoyl]isoxazole-3-carboxylate (Compound 16),

ethyl 5-cyclopropyl-4-[4-methylthio-2-(1-pyrazolylmethyl)benzoyl]isoxazole-3-carboxylate (Compound 82),

ethyl 4-[3,4-dichloro-2-(1,2,4-triazol-1-ylmethyl)benzoyl]-5-cyclopropylisoxazole-3-carboxylate (Compound 136),

ethyl 4-[4-bromo-2-(1,2,4-triazol-1-ylmethyl)benzoyl]-5-cyclopropylisoxazole-3-carboxylate (Compound 48),

ethyl 4-[4-bromo-2-(2-methylthio-1-imidazolylmethyl)benzoyl]-5-cyclopropylisoxazole-3-carboxylate (Compound 326),

ethyl 4-[4-bromo-2-(3-methylthio-1,2,4-triazol-1-ylmethyl)benzoyl]-5-cyclopropylisoxazole-3-carboxylate (Compound 327),

ethyl 5-cyclopropyl-4-[2-(2-methylthio-1-imidazolylmethyl)benzoyl]isoxazole-3-carboxylate (Compound 372),

ethyl 5-cyclopropyl-4-[2-(3-methylthio-1,2,4-triazol-1-ylmethyl)benzoyl]isoxazole-3-carboxylate (Compound 328),

4-[4-bromo-2-(3-*tert*-butyl-5-methylthio-1,2,4-triazol-1-ylmethyl)benzoyl]5-cyclopropylisoxazole (Compound 329),

4-[4-bromo-2-(5-cyclopropyl-3-methylthio-1,2,4-triazol-1-ylmethyl)benzoyl]5-cyclopropylisoxazole (Compound 330), and

ethyl 5-cyclopropyl-4-[2-(3-methylthio-1,2,4-triazol-1-ylmethyl)-4-(trifluoromethyl)benzoyl]isoxazole-3-carboxylate (Compound 331).

Example 2

Dimethylformamide dimethyl acetal (2.4ml) was added to a solution of 3-cyclopropyl-1-[4-methylthio-2-(1-pyrazolylmethyl)phenyl]-propan-1,3-dione in toluene at room temperature. The mixture was refluxed for 2 hours, evaporated and redissolved in ethanol. Hydroxylamine hydrochloride (0.74g) was added and the reaction

mixture stirred at ambient temperature for 2 hours. Water was added and the mixture extracted with dichloromethane. The extract was washed with brine, dried over anhydrous magnesium sulphate and evaporated. The residue was purified by silica gel chromatography using n-hexane/ethyl acetate as eluent to give 5-cyclopropyl-4-[4-methylthio-2-(1-pyrazolylmethyl)benzoyl]isoxazole (Compound 73, 1.82g).

The following compounds were prepared in a similar manner:

5-cyclopropyl-4-[2-(3,5-dimethylpyrazol-1-ylmethyl)-4-(methylthio)benzoyl]isoxazole (Compound 74),

4-[3,4-dichloro-2-(1-pyrazolylmethyl)benzoyl]-5-cyclopropylisoxazole (Compound 128),

4-[3,4-dichloro-2-(1,2,4-triazol-1-ylmethyl)benzoyl]-5-cyclopropylisoxazole (Compound 127),

4-[4-bromo-2-(1-pyrazolylmethyl)benzoyl]-5-cyclopropylisoxazole (Compound 29),

4-[4-bromo-2-(1,2,4-triazol-1-ylmethyl)benzoyl]-5-cyclopropylisoxazole (Compound 28),

5-cyclopropyl-4-[2-(3-methylpyrazol-1-ylmethyl)-4-(methylthio)benzoyl]isoxazole and 5-cyclopropyl-4-[2-(5-methylpyrazol-1-ylmethyl)-4-(methylthio)benzoyl]isoxazole as a mixture (Compounds 75 and 76),

5-cyclopropyl-4-[2-(3-methylthio-1,2,4-triazol-1-ylmethyl)benzoyl]isoxazole (Compound 332),

5-cyclopropyl-4-[2-(5-methylthio-1,2,4-triazol-1-ylmethyl)benzoyl]isoxazole (Compound 333),

4-[4-bromo-2-(3-methylthio-1,2,4-triazol-1-ylmethyl)benzoyl]-5-cyclopropylisoxazole (Compound 334),

4-[4-bromo-2-(5-methylthio-1,2,4-triazol-1-ylmethyl)benzoyl]-5-cyclopropylisoxazole (Compound 335),

5-cyclopropyl-4-[3,4-dichloro-2-(3-methylthio-1,2,4-triazol-1-ylmethyl)benzoyl]isoxazole (Compound 336),

5-cyclopropyl-4-[3,4-dichloro-2-(5-methylthio-1,2,4-triazol-1-ylmethyl)benzoyl]isoxazole (Compound 337),

5-cyclopropyl-4-[2,4-dichloro-3-(1,2,4-triazol-1-ylmethyl)benzoyl]isoxazole (Compound 262),

5-cyclopropyl-4-[2,4-dichloro-3-(1-pyrazolylmethyl)benzoyl]isoxazole (Compound 263),

5-cyclopropyl-4-{2-[1-(1,2,4-triazol-1-yl)ethyl]benzoyl}isoxazole (Compound 346),

5-cyclopropyl-4-{4-fluoro-2-[1-(1,2,4-triazol-1-yl)ethyl]benzoyl}isoxazole (Compound 347, mp 112-114),

5-cyclopropyl-4-{4-methylthio-2-[1-(1,2,4-triazol-1-yl)ethyl]benzoyl}isoxazole (Compound 348),

5-cyclopropyl-4-{2,2-difluoro-4-[1-(1,2,4-triazol-1-yl)ethyl]-1,3-benzodioxol-5-oyl}isoxazole (Compound 349, m.p.63-65 °C),

4-{4-bromo-2-[1-(1,2,4-triazol-1-yl)propyl]benzoyl}-5-cyclopropylisoxazole (Compound 350), and

5-cyclopropyl-4-{4-fluoro-2-[2-(1,2,4-triazol-1-yl)ethyl]benzoyl}isoxazole (Compound 351).

Example 3

To a solution of 5-cyclopropyl-4-[4-methylthio-2-(1-pyrazolylmethyl)benzoyl]isoxazole (0.60g) in dichloromethane, m-chloroperoxybenzoic acid (0.32g) was added at 0-5°C. The mixture was stirred at room temperature for 2 hours and quenched with an aqueous solution of sodium sulphite (1g) with stirring. The organic layer was washed with potassium carbonate solution, dried over anhydrous magnesium sulphate and evaporated. The residue was purified by silica gel chromatography using n-hexane/ethyl acetate as eluent to give 5-cyclopropyl-4-[4-methylsulphinyl-2-(1-pyrazolylmethyl)benzoyl]isoxazole (Compound 199, 0.65g).

The following compounds were prepared in a similar manner:

ethyl 5-cyclopropyl-4-[4-methylsulphonyl-2-(1-pyrazolylmethyl)-benzoyl]isoxazole-3-carboxylate (Compound 219),

ethyl 5-cyclopropyl-4-[2-(3,5-dimethylpyrazol-1-ylmethyl)-4-(methylsulphinyl)benzoyl]isoxazole-3-carboxylate (Compound 200),

ethyl 5-cyclopropyl-4-[2-(3,5-dimethylpyrazol-1-ylmethyl)-4-(methylsulphonyl)benzoyl]isoxazole-3-carboxylate (Compound 211),

4-[4-bromo-2-(3-methylsulphinyl-1,2,4-triazol-1-ylmethyl)benzoyl]-5-cyclopropylisoxazole (Compound 338),

5-cyclopropyl-4-[3,4-dichloro-2-(3-methylsulphinyl-1,2,4-triazol-1-ylmethyl)benzoyl]isoxazole (Compound 339),

5-cyclopropyl-4-[3,4-dichloro-2-(5-methylsulphinyl-1,2,4-triazol-1-ylmethyl)benzoyl]isoxazole (Compound 340),

ethyl 5-cyclopropyl-4-[3,4-dichloro-2-(3-methylsulphinyl-1,2,4-triazol-1-ylmethyl)benzoyl]isoxazole-3-carboxylate (Compound 341),

ethyl 5-cyclopropyl-4-[3,4-dichloro-2-(5-methylsulphinyl-1,2,4-triazol-1-ylmethyl)benzoyl]isoxazole-3-carboxylate (Compound 342),

ethyl 4-[4-bromo-2-(3-*tert*-butyl-5-methylsulphinyl-1,2,4-triazol-1-ylmethyl)benzoyl]-5-cyclopropylisoxazole-3-carboxylate (Compound 343),

ethyl 4-[4-bromo-2-(5-cyclopropyl-3-methylsulphinyl-1,2,4-triazol-1-ylmethyl)benzoyl]-5-cyclopropylisoxazole-3-carboxylate (Compound 344), and

5-cyclopropyl-4-{4-methylsulphinyl-2-[1-(1,2,4-triazol-1-yl)ethyl]benzoyl}isoxazole (Compound 345).

Similarly prepared but employing an excess of m-chloroperoxybenzoic acid (2.2 equivalents) were:

5-cyclopropyl-4-[4-methylsulphonyl-2-(1-pyrazolylmethyl)benzoyl]isoxazole, (Compound 210),

5-cyclopropyl-4-[2-(3-methylsulphonyl-1,2,4-triazol-1-ylmethyl)benzoyl]isoxazole (Compound 352),

4-[4-bromo-2-(3-methylsulphonyl-1,2,4-triazol-1-ylmethyl)benzoyl]-5-cyclopropylisoxazole (Compound 353),

5-cyclopropyl-4-[3,4-dichloro-2-(3-methylsulphonyl-1,2,4-triazol-1-ylmethyl)benzoyl]isoxazole (Compound 354),

5-cyclopropyl-4-[2-(5-methylsulphonyl-1,2,4-triazol-1-ylmethyl)benzoyl]isoxazole (Compound 355),

ethyl 5-cyclopropyl-4-[3,4-dichloro-2-(3-methylsulphonyl-1,2,4-triazol-1-ylmethyl)benzoyl]isoxazole-3-carboxylic acid (Compound 356),

ethyl 4-[4-bromo-2-(3-*tert*-butyl-5-methylsulphonyl-1,2,4-triazol-1-ylmethyl)benzoyl]-5-cyclopropylisoxazole-3-carboxylate (Compound 357),

ethyl 4-[4-bromo-2-(5-cyclopropyl-3-methylsulphonyl-1,2,4-triazol-1-ylmethyl)benzoyl]-5-cyclopropylisoxazole-3-carboxylate (Compound 358),

ethyl 5-cyclopropyl-4-[2-(3-methylsulphonyl-1,2,4-triazol-1-ylmethyl)-4-(trifluoromethyl)benzoyl]isoxazole-3-carboxylate (Compound 359),

ethyl 5-cyclopropyl-4-[2-(5-methylsulphonyl-1,2,4-triazol-1-ylmethyl)-4-(trifluoromethyl)benzoyl]isoxazole-3-carboxylate (Compound 360), and

5-cyclopropyl-4-{4-methylsulphonyl-2-[1-(1,2,4-triazol-1-yl)ethyl]benzoyl}isoxazole (Compound 361).

Example 4

By proceeding according to the method described in reference Example 1 below, the following compounds were prepared from the appropriately substituted starting materials:

ethyl 5-cyclopropyl-4-[3,4-dichloro-2-(3-methylthio-1,2,4-triazol-1-ylmethyl)benzoyl]isoxazole-3-carboxylate (Compound 362),

ethyl 4-[4-bromo-2-(5-methylthio-1,2,4-triazol-1-ylmethyl)benzoyl]-5-cyclopropylisoxazole-3-carboxylate (Compound 363),

ethyl 4-[4-bromo-2-(3-*tert*-butyl-5-methylthio-1,2,4-triazol-1-ylmethyl)benzoyl]-5-cyclopropylisoxazole-3-carboxylate (Compound 364),

ethyl 4-[4-bromo-2-(5-cyclopropyl-3-methylthio-1,2,4-triazol-1-ylmethyl)benzoyl]-5-cyclopropylisoxazole-3-carboxylate (Compound 365),

ethyl 4-[4-bromo-2-(3-cyclopropyl-5-methylthio-1,2,4-triazol-1-ylmethyl)benzoyl]-5-cyclopropylisoxazole-3-carboxylate (Compound 366),

ethyl 4-[4-bromo-2-(3-isopropyl-5-methylthio-1,2,4-triazol-1-ylmethyl)benzoyl]-5-cyclopropylisoxazole-3-carboxylate (Compound 367), and

ethyl 4-[4-bromo-2-(5-isopropyl-3-methylthio-1,2,4-triazol-1-ylmethyl)benzoyl]-5-cyclopropylisoxazole-3-carboxylate (Compound 368).

Example 5

A mixture of sodium acetate (0.41g) and hydroxylamine hydrochloride (0.35g) was added in one portion to a stirred solution of 3-{4-bromo-2-[1-(1,2,4-triazol-1-yl)ethyl]phenyl}-1-cyclopropyl-2-

ethoxymethylene-1,3-propandione (1.9g) in ethanol at ambient temperature and stirred at ambient temperature for 3 hours. Water was added and the mixture extracted (dichloromethane) and washed successively with brine and water, dried (magnesium sulphate), evaporated and purified by silica gel chromatography using n-hexane / ethyl acetate as eluent. Recrystallisation from hot ether gave 4-{4-bromo-2-[1-(1,2,4-triazol-1-yl)ethyl]benzoyl}-5-cyclopropylisoxazole (Compound 369, 0.30g), m.p. 125-126°C.

Example 6

Triethylamine (0.3g) was added to a solution of 4-[4-bromo-2-(pyrazol-1-ylmethyl)benzoyl]-5-cyclopropylisoxazole (0.5g) in dichloromethane at room temperature and stirred for 2 hours. Hydrochloric acid (10%) was added and the mixture extracted with dichloromethane. The organic layer was washed with brine, dried (magnesium sulphate) and evaporated togive 1-[4-bromo-2-(1-pyrazolylmethyl)]phenyl-2-cyano-3-cyclopropylpropan-1,3-dione (Compound 370, 0.5g).

Example 7

A solution of dimethylformamide dimethyl acetal (1.22ml) and 1-[4-bromo-2-(1,2,4-triazol-1-ylmethyl)phenyl]-3-cyclopropylpropan-1,3-dione in dry toluene was stirred for 18 hours at 90°C, evaporated and redissolved in ethanol. Hydroxylamine hydrochloride (0.51g) was added and the reaction mixture stirred at ambient temperature for 3 hours. Water and dichloromethane were added and the organic phase washed with brine, dried over anhydrous magnesium sulphate and evaporated. The residue was purified by silica gel chromatography using hexane / ethyl acetate to give 5-{4-bromo-2-[1-(1,2,4-triazol-1-yl)propyl]phenyl}-4-(cyclopropylcarbonyl)isoxazole (Compound 371, 0.35g).

Reference Example 1

A mixture of magnesium (0.53g) in methanol was refluxed to give a clear solution. 3-Cyclopropyl-1-(2-methyl-4-trifluoromethylphenyl)-propan-1,3-dione (5.42g) was added to the stirred solution and the mixture heated at reflux for 1 hour and then evaporated. Dichloromethane was added to the residue, followed portionwise by

ethyl chloroximidoacetate (3.35g) at 10°C. The reaction mixture was stirred at ambient temperature for 6 hours, then hydrochloric acid (1M) was added and the mixture extracted with dichloromethane. The extracts were washed with brine, dried over anhydrous MgSO4 and evaporated in vacuo. Purification by silica gel chromatography (using n-hexane/ethyl acetate 5:1 as eluent) gave ethyl 5-cyclopropyl-4-(2-methyl-4-trifluoromethylbenzoyl)isoxazole-3-carboxylate (4.80g), NMR 1.13(1H,t), 1.24(2H,m), 1.33(2H,m), 2.40(1H,m), 2.57(3H,s), 4.03(2H,q), 7.4-7.6(3H).

The following compounds were prepared in a similar manner:

ethyl 5-cyclopropyl-4-(2-methylbenzoyl)isoxazole-3-carboxylate, NMR 1.1-1.4(7H,m), 2.28(1H,m), 2.53(3H,s), 4.03(2H,q), 7.18-7.45(4H,m),

ethyl 5-cyclopropyl-4-[2-methyl-4-(methylthio)benzoyl]isoxazole-3-carboxylate, NMR 1.18(3H,t), 1.15-1.2(2H,m), 1.25-1.32(2H,m), 2.26(1H,m), 2.50(3H,s), 2.56(3H,s), 4.12(2H,q), 7.02(1H,dd), 7.12(1H,d), 7.32(1H,t),

ethyl 4-(3,4-dichloro-2-methylbenzoyl)-5-cyclopropylisoxazole-3-carboxylate, NMR 1.98(3H,t), 1.18-1.23(2H,m), 2.3-2.35(2H,m), 2.38(1H,m), 2.54(3H,s), 4.1(2H,q), 7.18(1H,d), 7.36(1H,d),

ethyl 4-(4-bromo-2-methylbenzoyl)-5-cyclopropylisoxazole-3-carboxylate, NMR 1.17(3H,t), 1.15-1.34(4H,m), 2.3(1H,m), 2.51(3H,s), 4.11(2H,q), 7.25(1H,d), 7.38(1H,dd), 7.48(1H,d), and

ethyl 5-cyclopropyl-4-[2-(5-methylthio-1,2,4-triazol-1-ylmethyl)-4-trifluoromethylbenzoyl]isoxazole-3-carboxylate.

Reference Example 2

To a stirred suspension of sodium hydride (4.92g, 60% in mineral oil) in tetrahydrofuran was added a mixture of cyclopropyl methylketone (9.61g) and methyl 4-methylthio-2-(1-pyrazolylmethyl)benzoate (12.47g) in tetrahydrofuran at 60-65°C. The reaction mixture was stirred at 65°C for 4 hours, poured into hydrochloric acid (1M) and ice and extracted with ethyl acetate. The organic layer was washed with brine, dried over anhydrous MgSO4 and evaporated. The residue was purified by silica gel chromatography using n-hexane/ethyl acetate (50:1) as eluent to give 3-cyclopropyl-1-[4-methylthio-2-(1-pyrazolylmethyl)phenyl]-propan-1,3-

dione (11.55g), NMR: 1.00(2H,m), 1.21(2H,m), 1.73(1H,m), 2.38(3H,s), 5.62(2H,s), 5.98(1H), 6.28(1H), 6.72(1H), 7.16(1H), 7.46(1H), 7.48(1H), 7.57(1H).

The following compounds were prepared in a similar manner:

3-cyclopropyl-1-(2-methylphenyl)propan-1,3-dione, NMR 1.0(2H,m), 1.21(2H,m), 2.5(3H,s), 5.93(1H,s), 7.2-7.6(4H),

1-(3,4-dichloro-2-methylphenyl)-3-cyclopropylpropan-1,3-dione, NMR 0.98-1.15(2H,m), 1.19-1.27(2H,m), 1.83(1H,m), 2.53(3H,s), 5.83(1H,s), 7.25(1H,d), 7.36(1H,d),

3-cyclopropyl-1-[2-(3,5-dimethylpyrazol-1-ylmethyl)-4-(methylthio)phenyl]propan-1,3-dione, NMR 0.95-1.15(2H,m), 1.18-1.23(2H,m), 2.12(3H,s), 2.28(3H,s), 2.32(3H,s), 5.5(2H,s), 5.88(1H), 6.02(1H), 6.3(1H), 7.1(1H), 7.43(1H),

3-cyclopropyl-1[2-(3-methylpyrazol-1-ylmethyl)-4-(methylthio)phenyl]propan-1,3-dione and 3-cyclopropyl-1[2-(5-methylpyrazol-1-ylmethyl)-4-(methylthio)phenyl]propan-1,3-dione as a mixture used directly in the next stage,

1-[3,4-dichloro-2-(1-pyrazolylmethyl)phenyl]-3-cyclopropylpropan-1,3-dione,

1-[3,4-dichloro-2-(1,2,4-triazol-1-ylmethyl)phenyl]-3-cyclopropylpropan-1,3-dione, NMR 1.0-1.1(2H,m), 1.2-1.3(2H,m), 1.7(1H,m), 5.72(2H,s), 5.98(1H,s), 7.42(2H,d), 7.59(1H,d), 7.9(1H,s), 8.09(1H,s),

1-[4-bromo-2-(1-pyrazolylmethyl)phenyl]-3-cyclopropylpropan-1,3-dione,

1-[4-bromo-2-(1,2,4-triazol-1-ylmethyl)phenyl]-3-cyclopropylpropan-1,3-dione, NMR 1.0-1.08(2H,m), 1.2-1.27(2H,m), 1.72(1H,m), 5.62(2H,s), 5.98(1H,s), 7.38(1H,d), 7.43(1H,d), 7.52(1H,dd), 7.98(1H,s), 8.2(1H,s),

3-cyclopropyl-1-{4-methylthio-2-[1-(1,2,4-triazol-1-yl)ethyl]phenyl}propan-1,3-dione, NMR 1.0-1.2(4H,m), 1.7(1H,m), 1.9(3H,d), 2.4(3H,s), 6.0(2H,s), 6.3(1H,q), 7.2(1H,s), 7.2(1H,d), 7.4(1H,d)8.0(1H,s), 8.3(1H,s),

3-cyclopropyl-1-{4-fluoro-2-[1-(1,2,4-triazol-1-yl)ethyl]phenyl}propan-1,3-dione, NMR 1.0-1.2(4H,m), 1.7(1H,m),

1.9(3H,d), 6.0(1H,s), 6.3(1H,q), 7.1(2H,m) 7.5(1H,m), 8.0(1H,s), 8.4(1H,s),

3-cyclopropyl-1-{2-[1-(1,2,4-triazol-1-yl)ethyl]phenyl}propan-1,3-dione, NMR 1.0-1.2(4H,m), 1.7(1H,m), 1.9(3H,d), 6.0(2H,s), 6.2(1H,q), 7.4(4H,m), 8.0(1H,s), 8.2(1H,s),

3-cyclopropyl-1-{2,2-difluoro-4-[1-(1,2,4-triazol-1-yl)ethyl]-1,3-benzodioxol-5-yl}propan-1,3-dione, NMR 1.0-1.3(4H,m), 1.7(1H,m), 1.9(3H,d), 6.0(2H,s), 6.2(1H,q), 7.1(1H,d), 7.3(1H,d), 8.0(1H,s), 8.4(1H,s),

1-{4-bromo-2-[1-(1,2,4-triazol-1-yl)propyl]phenyl}-3-cyclopropylpropan-1,3-dione, NMR 0.9(3H,t), 1.1(2H,m), 1.4(2H,m), 1.7(1H,m), 2.2(1H,m), 2.5(1H,m), 6.0(3H,m), 7.3(1H,d), 7.5(1H,d), 7.8(1H,s), 8.1(1H,s), 8.4(1H,s),

3-cyclopropyl-1-{4-fluoro-2-[2-(1,2,4-triazol-1-yl)ethyl]phenyl}propan-1,3-dione, NMR 0.9(2H,m), 1.1(2H,m), 1.7(1H,m), 3.3(2H,t), 4.4(2H,t), 5.9(2H,s), 6.8(1H,d), 6.9(1H,t), 7.4(1H,m), 7.7(1H,s), 7.9(1H,s),

1-[4-bromo-2-(5-methylthio-1,2,4-triazol-1-ylmethyl)phenyl]-3-cyclopropylpropan-1,3-dione, NMR 1.04(2H,m), 1.22(2H,m), 1.75(1H,m), 2.69(3H,s), 5.54(2H,s),6.01(1H,s), 7.02(1H,d), 7.42(1H,d), 7.49(1H,dd), 7.91(1H,s),

1-[4-bromo-2-(3-methylthio-1,2,4-triazol-1-ylmethyl)phenyl]-3-cyclopropylpropan-1,3-dione, NMR 1.04(2H,m), 1.24(2H,m), 1.73(1H,m), 2.59(3H,s), 5.53(2H,s), 5.99(1H,s), 7.41(1H,d), 7.43(1H,d), 7.53(1H,dd), 8.09(1H,s),

3-cyclopropyl-1-[3,4-dichloro-2-(3-methylthio-1,2,4-triazol-1-ylmethyl)phenyl]propan-1,3-dione, NMR 1.04(2H,m), 1.25(2H,m),1.70(1H,m), 2.55(3H,s), 5.68(2H,s), 5.98(1H,s), 7.40(1H,d), 7.57(1H,d), 7.96(1H,s),

3-cyclopropyl-1-[3,4-dichloro-2-(5-methylthio-1,2,4-triazol-1-ylmethyl)phenyl]propan-1,3-dione, NMR 1.04(2H,m), 1.25(2H,m), 1.70(1H,m), 2.71(3H,s), 5.51(2H,s), 5.95(1H,s), 7.40(1H,d), 7.55(1H,d), 7.79(1H,s),

3-cyclopropyl-1-[(3-methylthio-1,2,4-triazol-1-ylmethyl)phenyl]propan-1,3-dione, NMR 1.03(2H,m), 1.22(2H,m),

2.58(3H,s), 5.56(2H,s), 6.02(1H,s), 7.25(1H.dd), 7.36-7.48(2H,m), 7.55(1H,dd), 8.06(1H,s),

1-[4-bromo-2-(3-*tert*-butyl-5-methylthio-1,2,4-triazol-1-ylmethyl)phenyl]-3-cyclopropylpropan-1,3-dione, NMR 1.02(2H,m), 1.23(2H,m), 1.36(9H,s), 1.75(1H,m), 2.63(3H,s), 5.52(2H,s), 6.02(1H,s), 6.94(1H,d), 7.40(1H,d), 7.46(1H,dd),

3-cyclopropyl-1-[2-(5-methylthio-1,2,4-triazol-1-yl)methyl]phenyl-propan-1,3-dione,

1-[4-bromo-2-(5-cyclopropyl-3-methythio-1,2,4- triazol-1-ylmethyl)phenyl]-3-cyclopropylpropan-1,3-dione,

1-[4-bromo-2-(3-cyclopropyl-5-methythio-1,2,4-triazol-1-ylmethyl)phenyl]-3-cyclopropylpropan-1,3-dione,

1-[4-bromo-2-(3-isopropyl-5-methythio-1,2,4-triazol-1-ylmethyl)phenyl]-3-cyclopropylpropan-1,3-dione,

1-[4-bromo-2-(5-isopropyl-3-methythio-1,2,4-triazol-1-ylmethyl)phenyl]-3-cyclopropylpropan-1,3-dione,

3-cyclopropyl-1-[2,4-dichloro-3-(1-pyrazolylmethyl)phenyl]propan-1,3-dione,

3-cyclopropyl-1-[2,4-dichloro-3-(1,2,4-triazol-1-ylmethyl)phenyl]propan-1,3-dione, and

3-cyclopropyl-1-[2-(5-methylthio-1,2,4-triazol-1-ylmethyl)-4-trifluoromethylphenyl]propan-1,3-dione.

Reference Example 3

To a solution of methyl 4-fluoro-2-methylbenzoate (5.5g) in carbon tetrachloride, was added N-bromosuccinimide (7.0g) and benzoylperoxide (0.05g) at room temperature. The reaction mixture was exposed to the light of an ordinary 300W light bulb placed 5-6 cm from the flask for 2 hours under reflux conditions. The reaction mixture was cooled to room temperature, succinimide removed by filtration and the filtrate evaporated. N,N-Dimethylformamide was added to the residue and this solution added dropwise at room temperature to a solution of pyrazole (2.72g) and sodium hydride (60% in mineral oil; 1.6g) in N,N-dimethylformamide. The reaction mixture was stirred at ambient temperature for 5 hours, then sodium methanethiolate added portionwise at room temperature. The reaction mixture was stirred for 6 hours, then

water and ethyl acetate added. The organic layer was washed with brine, dried over anhydrous MgSO4 and evaporated. The residue was purified by silica gel chromatography using n-hexane/ethyl acetate (5:1) as eluent to give methyl 2-(pyrazol-1-ylmethyl)-4(methylthio)benzoate (5.22g), NMR: 2.33(3H,s), 3.90(3H,s), 5.78(2H,s), 6.32(1H), 6.50(1H,dd), 7.14(1H,dd), 7.50(1H), 7.59(1H), 7.92(1H,d).

The following compounds were prepared in a similar manner:

methyl 2-(3,5-dimethylpyrazol-1-ylmethyl)-4-(methylthio)benzoate,

methyl 2-(3-methylpyrazol-1-ylmethyl)-4-(methylthio)benzoate and methyl 2-(5-methylpyrazol-1-ylmethyl)-4-(methylthio)benzoate as a mixture, used directly in the next stage,

methyl 3,4-dichloro-2-(1-pyrazolylmethyl)benzoate, NMR 3.9(3H,s), 5.92(2H,s), 6.2(1H), 7.4(1H), 7.49(1H), 7.53(1H,d), 7.78(1H,d),

methyl 3,4-dichloro-2-(1,2,4-triazol-1-ylmethyl)benzoate, NMR 3.91(3H,s), 6.0(2H,s), 7.6(1H,d), 7.86(1H,d), 7.88(1H,s), 8.17(1H,s),

methyl 4-bromo-2-(1-pyrazolylmethyl)benzoate, NMR 3.9(3H,s), 5.75(2H,s), 6.32(1H), 6.89(1H), 7.48(1H,dd), 7.52(1H,s), 7.6(1H), 7.88(1H,d),

methyl 4-bromo-2-(1,2,4-triazol-1-ylmethyl)benzoate, NMR 3.9(3H,s), 5.8(2H,s), 7.33(1H,d), 7.56(1H,dd), 7.9(1H,d), 7.98(1H,s), 8.27(1H,s),

1.9(3H,d), 2.4(3H,s), 3.9(3H,s), 6.8(1H,q), 7.1(1H,t), 7.1(1H,d), 7.9(1H,d), 8.0(1H,s), 8.4(1H,s),

methyl 2-(3-methylthio-1,2,4-triazol-1-ylmethyl)benzoate, NMR 2.58(s,3H), 3.92(s,3H), 5.72(s,2H), 7.21(dd,1H), 7.36-7.57(m,2H), 8.03(dd,1H), methyl 4-bromo-2-(5-methylthio-1,2,4-triazol-1-ylmethyl)benzoate, NMR 2.70(3H,s), 3.93(3H,s), 5.72(2H,s), 6.86(1H,d), 7.51(1H,dd), 7.92(1H,d), 7.95(1H,s),

methyl 4-bromo-2-(3-methylthio-1,2,4-triazol-1-ylmethyl)benzoate, NMR 2.59(3H,s), 3.91(3H,s), 5.69(2H,s), 7.39(1H,d), 7.55(1H,dd), 7.90(1H,d), 8.18(1H,s),

methyl 3,4-dichloro-2-(3-methylthio-1,2,4-triazol-1-ylmethyl)benzoate, NMR 2.54(3H,s), 3.92(3H,s), 5.92(2H,s), 7.58(1H,d), 7.82(1H,d), 8.02(1H,s),

methyl 3,4-dichloro-2-(5-methylthio-1,2,4-triazol-1-ylmethyl)benzoate, NMR 2.73(3H,s), 3.89(3H,s), 5.79(2H,s), 7.58(1H,d), 7.76(1H,s), 7.85(1H,d),

methyl 4-bromo-2-(5-cyclopropyl-3-methylthio-1,2,4-triazol-1-ylmethyl)benzoate, NMR 0.99(2H,m), 1.10(2H,m), 1.71(1H,m), 2.56(3H,s), 3.93(3H,s), 5.81(2H,s), 6.95(1H,d), 7.52(1H,dd), 7.91(1H,d),

methyl 4-bromo-2-(3-cyclopropyl-5-methylthio-1,2,4-triazol-1-ylmethyl)benzoate, NMR 0.97(4H,m), 2.03(1H,m), 2.64(3H,s), 3.93(3H,s), 5.63(2H,s), 6.86(1H,d), 7.49(1H,dd), 7.89(1H,d),

methyl 4-bromo-2-(3-*tert*-butyl-5-methylthio-1,2,4-triazol-1-ylmethyl)benzoate, NMR 1.38(9H,s), 2.65(3H,s), 3.93(3H,s), 5.68(2H,s), 6.74(1H,d), 7.48(1H,dd), 7.88(1H,d),

methyl 4-bromo-2-(5-isopropyl-3-methylthio-1,2,4-triazol-1-ylmethyl)benzoate, NMR 1.26(6H,d), 2.57(3H,s), 2.94(1H,m), 3.92(3H,s), 5.71(2H,s), 8.86(1H,d), 7.50(1H,dd), 7.90(1H,d),

methyl 4-bromo-2-(3-isopropyl-5-methylthio-1,2,4-triazol-1-ylmethyl)benzoate, NMR 1.35(6H,m), 2.66(3H,s), 3.07(1H,m), 3.93(3H,s), 5.67(2H,s), 6.78(1H,d), 7.48(1H,dd), 7.89(1H,d),

methyl 2-(5-methythio-1,2,4-triazol-1-ylmethyl)benzoate,

methyl 2-(5-methylthio-1,2,4-triazol-1-ylmethyl)-4-trifluoromethylbenzoate,

methyl 2,4-dichloro-3-(1-pyrazolylmethyl)benzoate, and

methyl 2,4-dichloro-3-(1,2,4-triazol-1-ylmethyl)benzoate.

Reference Example 4

Oxalyl chloride (2 ml) was added to 2-methyl-4-trifluoromethylbenzoic acid (2g) stirred in dichloromethane. The mixture was heated at reflux for 4 hours and evaporated. Toluene was added and the solution re-evaporated to give the corresponding benzoyl chloride. A suspension of magnesium (0.24 g) in methanol was stirred and heated at reflux for 0.5 hours. t-Butyl 3-cyclopropyl-3-oxopropionate (1.8 g) was added and the mixture was heated at reflux for 0.5 hours. The mixture was cooled and evaporated. Toluene was added and the mixture re-evaporated. The residue was redissolved in toluene and treated with a toluene solution of the above benzoyl chloride. The mixture was stirred

at room temperature for 19 hours, then hydrochloric acid (2 M) added with stirring for a further 1 hour. The organic phase was washed with water, dried (magnesium sulphate) and treated with 4-toluenesulphonic acid (0.25 g). The mixture was stirred and heated at reflux for 2 hours, cooled, washed with water, dried (magnesium sulphate) and evaporated to give 3-cyclopropyl-1-(2-methyl-4-trifluoromethylphenyl)propan-1,3-dione, NMR 0.97(2H,m), 1.15(2H,m), 1.7(1H,m), 2.49(3H,s), 5.87(1H,s), 7.15(1H,m), 7.4(1H,d), 7.47(1H,d), 15.8(1H,br).

Reference Example 5

A solution containing 3-{4-bromo-2-[1-(1,2,4-triazol-1-yl)ethyl]phenyl}-1-cyclopropyl-1,3-propandione (2.2g), triethyl orthoformate (2ml) and acetic anhydride (1.74ml) was heated under reflux with exclusion of moisture for 8h. The solution was evaporated to dryness and purified by silica gel chromatography using n-hexane / ethyl acetate followed by ethanol as eluent to give 3-{4-bromo-2-[1-(1,2,4-triazol-1-yl)ethyl]phenyl}-1-cyclopropyl-2-ethoxymethylene-1,3-propandione (1.9g).

Refererence Example 6

N-Bromosuccinimide (3.85g) and a catalytic amount of azobisisobutyronitrile was added to a stirred solution of methyl 2-ethyl-4-bromobenzoate (5g) in tetrachloromethane. The solution was heated under reflux whilst exposed to a 300W light bulb placed 5-6 cm from the flask for 2 hours. The mixture was cooled to 0°C, filtered and the filtrate evaporated to dryness. A solution of 1,2,4-triazole (1.55g) in dimethylformamide was added dropwise to a suspension of sodium hydride (60% in mineral oil) in dimethylformamide. The mixture was stirred at 100°C for 45 minutes and cooled to 30°C. A solution of the residue from above in N,N-dimethylformamide was added dropwise to the triazole mixture, stirred at 100°C for a further 2 hour and cooled to 30°C. Water was added and the mixture extracted (ether) and the organic phase washed with brine and water, dried (magnesium sulphate) and evaporated. Trituration with cold ether gave methyl 4-bromo-2-[1-(1,2,4-triazol-1-yl)ethyl]benzoate (4.17g).

The following compounds were prepared in a similar manner:

methyl 2-[1-(1,2,4-triazol-1-yl)ethyl]-4-fluorobenzoate, NMR 1.9(3H,d), 3.9(3H,s), 6.8(1H,q), 7.0(2H,m), 8.0(1H,dd), 8.0(1H,s), 8.3(1H,s),

methyl 2-[1-(1,2,4-triazol-1-yl)ethyl]benzoate, NMR 2.0(3H,d), 3.9(3H,s), 6.7(1H,q), 7.3(1H,d), 7.4(1H,t), 7.5(1H,t), 8.0(1H,d), 8.0(1H,s), 8.2(1H,s),

methyl {2,2-difluoro-4-[1-(1,2,4-triazol-1-yl)ethyl]benzo[*d*][1,3]dioxol-5-yl}carboxylate, and

methyl 4-bromo-2-[1-(1,2,4-triazol-1-yl)propyl]benzoate.

Reference Example 7

A mixture of methyl 4-fluoro-2-vinylbenzoate (5.84g), 1,2,4-triazole (2.69g), potassium carbonate (0.45g) and dimethyl sulphoxide was stirred at 140°C for 30h, then cooled, poured into water and extracted with ethyl acetate. The extract was washed with water and brine, dried (magnesium sulphate), evaporated and purified by silica gel chromatography using ethyl acetate / methanol as eluent to give methyl 2-[2-(1,2,4-triazol-1-yl)ethyl]-4-fluorobenzoate, m.p. 80.7-81.7°C.

Reference Example 8

A solution of 2-(4-bromo-2-propylphenyl)-4,4-dimethyl-1,3-oxazoline (26g) in 6M hydrochloric acid was stirred under reflux for 24 hours. The solution was cooled to 0°C and the resultant solid filtered and dried under vacuum to give 4-bromo-2-propylbenzoic acid (20g), m.p. 141-143°C.

The following compounds were prepared in a similar manner:

2-ethyl-4-bromobenzoic acid,

2-ethyl-2-fluorobenzoic acid, m.p. 113.5 - 114.5°C, and

4-fluoro-2-vinylbenzoic acid, m.p. 124.4-124.8°C.

Reference Example 9

1-Iodopropane (1ml) was added to a stirred mixture of magnesium turnings (8.24g) in dry ether under nitrogen, and then heated to reflux. A solution of 1-iodopropane (31ml) in dry ether was added dropwise at such a rate as to maintain reflux. After an additional 1 hour at reflux the cooled mixture was added via a canula to a stirred solution of 2-(4-

bromo-2-fluorophenyl)-4,4-dimethyloxazoline (25g) in dry ether at below 25°C. The resultant mixture was stirred at reflux for 18 hours, cooled and poured into ice and 2M hydrochloric acid. The mixture was basified to pH11 with 10M sodium hydroxide solution, extracted (ethyl acetate), washed (water), dried (magnesium sulphate) and evaporated to give 2-(4-bromo-2-propylphenyl)-4,4-dimethyl-1,3-oxazoline (26g).

The following compounds were prepared in a similar manner:

2-(4-bromo-2-propylphenyl)-4,4-dimethyloxazoline,

4,4-dimethyl-2-(2-ethyl-4-fluorophenyl)oxazoline, and

4,4-dimethyl-2-(4-fluoro-2-vinylphenyl)oxazoline, NMR 1.32 (6H,s), 4.01 (2H,s), 5.31 (1H,d), 5.66 (1H,d), 6.90 (1H,m), 7.22 (1H,m), 7.43 (1H,m), 7.70 (1H,m).

Reference Example 10

A 2.5M solution of butyllithium in hexane (176ml) was added dropwise to a solution of 2,2-difluoro-1,3-benzodioxole-5-carboxylic acid (40.4g) in dry tetrahydrofuran at -78°C under nitrogen, maintaining below -65°C, and stirred at -78°C for 15 hours. A solution of iodoethane (80ml) in dry tetrahydrofuran was added dropwise below -70°C and then stirred at -75°C for 30 minutes, before allowing to warm to ambient temperature. After an additional 1 hour the mixture was added to a stirred solution of excess aqueous sodium hydroxide (2M) and the aqueous layer acidified (concentrated hydrochloric acid), cooled and the resultant solid collected, washed with water and dried *in vacuo* to give 2,2-difluoro-4-ethyl-1,3-benzodioxole-5-carboxylic acid (37.4g), m.p. 175-180°C.

Methyl benzoates were prepared by reaction of the corresponding benzoic acid derivatives with methanol by heating under reflux conditions in the presence of a strong acid (concentrated sulphuric acid).

According to a feature of the present invention, there is provided a method for controlling the growth of weeds (i.e. undesired vegetation) at a locus which comprises applying to the locus a herbicidally effective amount of at least one isoxazole or 2-cyano-1,3-dione derivative of formula (I) or an agriculturally acceptable salt thereof. For this purpose,

the isoxazole or 2-cyano-1,3-dione derivatives are normally used in the form of herbicidal compositions (i.e. in association with compatible diluents or carriers and/or surface active agents suitable for use in herbicidal compositions), for example as hereinafter described.

The compounds of formula (I) show herbicidal activity against dicotyledonous (i.e. broad-leafed) and monocotyledonous (i.e. grass) weeds by pre- and/or post-emergence application.

By the term "pre-emergence application" is meant application to the soil in which the weed seeds or seedlings are present before emergence of the weeds above the surface of the soil. By the term "post-emergence application" is meant application to the aerial or exposed portions of the weeds which have emerged above the surface of the soil.

For example, the compounds of formula (I) may be used to control the growth of:

broad-leafed weeds, for example, Abutilon theophrasti, Amaranthus retroflexus, Bidens pilosa, Chenopodium album, Galium aparine, Ipomoea spp. e.g. Ipomoea purpurea, Sesbania exaltata, Sinapis arvensis, Solanum nigrum and Xanthium strumarium, and

grass weeds, for example Alopecurus myosuroides, Avena fatua, Digitaria sanguinalis, Echinochloa crus-galli, Sorghum bicolor, Eleusine indica and Setaria spp, e.g. Setaria faberii or Setaria viridis, and

sedges, for example, Cyperus esculentus.

The amounts of compounds of formula (I) applied vary with the nature of the weeds, the compositions used, the time of application, the climatic and edaphic conditions and (when used to control the growth of weeds in crop-growing areas) the nature of the crops. When applied to a crop-growing area, the rate of application should be sufficient to control the growth of weeds without causing substantial permanent damage to the crop. In general, taking these factors into account, application rates between 0.01kg and 5kg of active material per hectare give good results. However, it is to be understood that higher or lower application rates may be used, depending upon the particular problem of weed control encountered.

The compounds of formula (I) may be used to control selectively the growth of weeds, for example to control the growth of those species hereinbefore mentioned, by pre- or post-emergence application in a

directional or non-directional fashion, e.g. by directional or non-directional spraying, to a locus of weed infestation which is an area used, or to be used, for growing crops, for example cereals, e.g. wheat, barley, oats, maize and rice, soya beans, field and dwarf beans, peas, lucerne, cotton, peanuts, flax, onions, carrots, cabbage, oilseed rape, sunflower, sugar beet, and permanent or sown grassland before or after sowing of the crop or before or after emergence of the crop. For the selective control of weeds at a locus of weed infestation which is an area used, or to be used, for growing of crops, e.g. the crops hereinbefore mentioned, application rates between 0.01kg and 4.0kg, and preferably between 0.01kg and 2.0kg, of active material per hectare are particularly suitable.

The compounds of formula (I) may also be used to control the growth of weeds, especially those indicated above, by pre- or post-emergence application in established orchards and other tree-growing areas, for example forests, woods and parks, and plantations, e.g. sugar cane, oil palm and rubber plantations. For this purpose they may be applied in a directional or non- directional fashion (e.g. by directional or non-directional spraying) to the weeds or to the soil in which they are expected to appear, before or after planting of the trees or plantations at application rates between 0.25kg and 5.0kg, and preferably between 0.5kg and 4.0kg of active material per hectare.

The compounds of formula (I) may also be used to control the growth of weeds, especially those indicated above, at loci which are not crop-growing areas but in which the control of weeds is nevertheless desirable.

Examples of such non-crop-growing areas include airfields, industrial sites, railways, roadside verges, the verges of rivers, irrigation and other waterways, scrublands and fallow or uncultivated land, in particular where it is desired to control the growth of weeds in order to reduce fire risks. When used for such purposes in which a total herbicidal effect is frequently desired, the active compounds are normally applied at dosage rates higher than those used in crop-growing areas as hereinbefore described. The precise dosage will depend upon the nature of the vegetation treated and the effect sought.

Pre- or post-emergence application, and preferably pre-emergence application, in a directional or non-directional fashion (e.g. by directional

or non-directional spraying) at application rates between 1.0kg and 20.0kg, and preferably between 5.0 and 10.0kg, of active material per hectare are particularly suitable for this purpose.

When used to control the growth of weeds by pre-emergence application, the compounds of formula (I) may be incorporated into the soil in which the weeds are expected to emerge. It will be appreciated that when the compounds of formula (I) are used to control the growth of weeds by post-emergence application, i.e. by application to the aerial or exposed portions of emerged weeds, the compounds of formula (I) will also normally come into contact with the soil and may also then exercise a pre-emergence control on later-germinating weeds in the soil.

Where especially prolonged weed control is required, the application of the compounds of formula (I) may be repeated if required.

According to a further feature of the present invention, there are provided compositions suitable for herbicidal use comprising one or more of the isoxazole or 2-cyano-1,3-dione derivatives of formula (I), in association with, and preferably homogeneously dispersed in, one or more compatible agriculturally- acceptable diluents or carriers and/or surface active agents [i.e. diluents or carriers and/or surface active agents of the type generally accepted in the art as being suitable for use in herbicidal compositions and which are compatible with compounds of formula (I)]. The term "homogeneously dispersed" is used to include compositions in which the compounds of formula (I) are dissolved in other components. The term "herbicidal compositions" is used in a broad sense to include not only compositions which are ready for use as herbicides but also concentrates which must be diluted before use. Preferably, the compositions contain from 0.05 to 90% by weight of one or more compounds of formula (I).

The herbicidal compositions may contain both a diluent or carrier and surface-active (e.g. wetting, dispersing, or emulsifying) agent. Surface-active agents which may be present in herbicidal compositions of the present invention may be of the ionic or non-ionic types, for example sulphoricinoleates, quaternary ammonium derivatives, products based on condensates of ethylene oxide with alkyl and polyaryl phenols, e.g. nonyl- or octyl-phenols, or carboxylic acid esters of anhydrosorbitols which have been rendered soluble by etherification of the free hydroxy

groups by condensation with ethylene oxide, alkali and alkaline earth metal salts of sulphuric acid esters and sulphonic acids such as dinonyl- and dioctyl-sodium sulphonosuccinates and alkali and alkaline earth metal salts of high molecular weight sulphonic acid derivatives such as sodium and calcium lignosulphonates and sodium and calcium alkylbenzene sulphonates.

Suitably, the herbicidal compositions according to the present invention may comprise up to 10% by weight, e.g. from 0.05% to 10% by weight, of surface-active agent but, if desired, herbicidal compositions according to the present invention may comprise higher proportions of surface-active agent, for example up to 15% by weight in liquid emulsifiable suspension concentrates and up to 25% by weight in liquid water soluble concentrates.

Examples of suitable solid diluents or carriers are aluminium silicate, talc, calcined magnesia, kieselguhr, tricalcium phosphate, powdered cork, absorbent carbon black and clays such as kaolin and bentonite. The solid compositions (which may take the form of dusts, granules or wettable powders) are preferably prepared by grinding the compounds of formula (I) with solid diluents or by impregnating the solid diluents or carriers with solutions of the compounds of formula (I) in volatile solvents, evaporating the solvents and, if necessary, grinding the products so as to obtain powders. Granular formulations may be prepared by absorbing the compounds of formula (I) (dissolved in suitable solvents, which may, if desired, be volatile) onto the solid diluents or carriers in granular form and, if desired, evaporating the solvents, or by granulating compositions in powder form obtained as described above. Solid herbicidal compositions, particularly wettable powders and granules, may contain wetting or dispersing agents (for example of the types described above), which may also, when solid, serve as diluents or carriers.

Liquid compositions according to the invention may take the form of aqueous, organic or aqueous-organic solutions, suspensions and emulsions which may incorporate a surface-active agent. Suitable liquid diluents for incorporation in the liquid compositions include water, glycols, tetrahydrofurfuryl alcohol, acetophenone, cyclohexanone, isophorone, toluene, xylene, mineral, animal and vegetable oils and light

aromatic and naphthenic fractions of petroleum (and mixtures of these diluents). Surface-active agents, which may be present in the liquid compositions, may be ionic or non-ionic (for example of the types described above) and may, when liquid, also serve as diluents or carriers.

Powders, dispersible granules and liquid compositions in the form of concentrates may be diluted with water or other suitable diluents, for example mineral or vegetable oils, particularly in the case of liquid concentrates in which the diluent or carrier is an oil, to give compositions ready for use.

Liquid concentrates in which the diluent or carrier is an oil may be used without further dilution using the electrostatic spray technique.

Herbicidal compositions according to the present invention may also contain, if desired, conventional adjuvants such as adhesives, protective colloids, thickeners, penetrating agents, spreading agents, stabilisers, sequestering agents, anti-caking agents, colouring agents and corrosion inhibitors. These adjuvants may also serve as carriers or diluents.

Unless otherwise specified, the following percentages are by weight. Preferred herbicidal compositions according to the present invention are

aqueous suspension concentrates which comprise from 10 to 70% of one or more compounds of formula I, from 2 to 10% of surface-active agent, from 0.1 to 5% of thickener and from 15 to 87.9% of water;

wettable powders which comprise from 10 to 90% of one or more compounds of formula I, from 2 to 10% of surface-active agent and from 8 to 88% of solid diluent or carrier;

water dispersible granules which comprise from 1 to 75%, e.g. 50 to 75%, of one or more compounds of formula (I), from 2 to 10% of surface-active agent and from 1 to 20%, e.g. 5-15%, of water soluble binder;

liquid emulsifiable suspension concentrates which comprise from 10 to 70% of one or more compounds of formula I, from 5 to 15% of surface-active agent, from 0.1 to 5% of thickener and from 10 to 84.9% of organic solvent, e.g. mineral oil;

granules which comprise from 1 to 90%, e.g. 2 to 10% of one or more compounds of formula (I), from 0.5 to 7%, e.g. 0.5 to 2%, of surface-active agent and from 3 to 98.5%, e.g. 88 to 97.5%, of granular carrier and

emulsifiable concentrates which comprise 0.05 to 90%, and preferably from 1 to 60% of one or more compounds of formula (I), from 0.01 to 10%, and preferably from 1 to 10%, of surface-active agent and from 9.99 to 99.94%, and preferably from 39 to 98.99%, of organic solvent.

Herbicidal compositions according to the present invention may also comprise the compounds of formula I in association with, and preferably homogeneously dispersed in, one or more other pesticidally active compounds and, if desired, one or more compatible pesticidally acceptable diluents or carriers, surface-active agents and conventional adjuvants as hereinbefore described.

Examples of other pesticidally active compounds which may be included in, or used in conjunction with, the herbicidal compositions of the present invention include herbicides, for example to increase the range of weed species controlled for example alachlor [2-chloro-2,6'-diethyl-N-(methoxy-methyl)-acetanilide], atrazine [2-chloro-4-ethylamino-6-isopropylamino-1,3,5-triazine], bromoxynil [3,5-dibromo-4-hydroxybenzonitrile], chlortoluron [N'-(3-chloro-4-methylphenyl)-N,N-dimethylurea], cyanazine [2-chloro-4-(1-cyano-1-methylethylamino)-6-ethylamino-1,3,5-triazine], 2,4-D [2,4-dichlorophenoxy-acetic acid], dicamba [3,6-dichloro-2-methoxybenzoic acid], difenzoquat [1,2- dimethyl-3,5-diphenyl-pyrazolium salts], flampropmethyl [methyl N-2-(N- benzoyl-3-chloro-4-fluoroanilino)-propionate], fluometuron [N'-(3-trifluoro- methylphenyl)-N,N-dimethylurea], isoproturon [N'-(4-isopropylphenyl)-N,N-dimethylurea], insecticides, e.g. synthetic pyrethroids, e.g permethrin and cypermethrin, and fungicides, e.g. carbamates, e.g. methyl N-(1-butyl-carbamoyl-benzimidazol-2-yl)carbamate, and triazoles e.g. 1-(4-chloro-phenoxy)-3,3-dimethyl-1-(1,2,4-triazol-1-yl)-butan-2-one.

Pesticidally active compounds and other biologically active materials which may be included in, or used in conjunction with, the herbicidal compositions of the present invention, for example those hereinbefore mentioned, and which are acids, may, if desired, be utilised in the form of conventional derivatives, for example alkali metal and amine salts and esters.

According to a further feature of the present invention there is provided an article of manufacture comprising at least one of the isoxazole or 2-cyano-1,3-dione derivatives of formula (I) or, as is preferred, a herbicidal composition as hereinbefore described, and preferably a herbicidal concentrate which must be diluted before use, comprising at least one of the isoxazole or 2-cyano-1,3-dione derivatives of formula (I) within a container for the aforesaid derivative or derivatives of formula I, or a said herbicidal composition, and instructions physically associated with the aforesaid container setting out the manner in which the aforesaid derivative or derivatives of formula I or herbicidal composition contained therein is to be used to control the growth of weeds. The containers will normally be of the types conventionally used for the storage of chemical substances which are solid at normal ambient temperatures and herbicidal compositions particularly in the form of concentrates, for example cans and drums of metal, which may be internally lacquered, and plastics materials, bottles or glass and plastics materials and, when the contents of the container is a solid, for example granular, herbicidal compositions, boxes, for example of cardboard, plastics materials and metal, or sacks. The containers will normally be of sufficient capacity to contain amounts of the isoxazole or 2-cyano-1,3-dione derivative or herbicidal compositions sufficient to treat at least one acre of ground to control the growth of weeds therein but will not exceed a size which is convenient for conventional methods of handling. The instructions will be physically associated with the container, for example by being printed directly thereon or on a label or tag affixed thereto. The directions will normally indicate that the contents of the container, after dilution if necessary, are to be applied to control the growth of weeds at rates of application between 0.1kg and 20kg of active material per hectare in the manner and for the purposes hereinbefore described.

The following Examples illustrate herbicidal compositions according to the present invention. The following trade marks appear in the Examples: Synperonic, Solvesso, Arylan, Arkopon, Sopropon, Tixosil, Soprophor, Attagel, Rhodorsil.

Example C1:

An emulsifiable concentrate is formed from:

Active ingredient (Compound 1)	20% w/v
N-Methylpyrrolidone (NMP)	25% w/v
Calcium dodecylbenzenesulphonate 70% (CaDDBS) (Arylan CA)	4% w/v
Nonylphenol ethylene oxide propylene oxide condensate (NPEOPO) (Synperonic NPE 1800)	6% w/v
Aromatic solvent (Solvesso)	to 100 volumes

by stirring NMP, active ingredient (Compound 1), CaDDBS, NPEOPO and Aromatic solvent until a clear solution is formed, and adjusting to volume with Aromatic solvent.

Example C2

A wettable powder is formed from:

Active ingredient (Compound 1)	50% w/w
Sodium dodecylbenzenesulphonate (Arylan SX85)	3% w/w
Sodium methyl oleoyl taurate (Arkopon T)	5% w/w
Sodium polycarboxylate (Sopropon T36)	1% w/w
Microfine silicon dioxide (Tixosil 38)	3% w/w
China clay	38% w/w

by blending the above ingredients together and grinding the mixture in an air jet mill.

Example C3

A suspension concentrate is formed from:

Active ingredient (Compound 1)	50% w/v
Antifreeze (Propylene glycol)	5% w/v
Ethoxylated tristyrylphenol phosphate (Soprophor FL)	0.5% w/v
Nonyl phenol 9 mole ethoxylate (Ethylan BCP)	0.5% w/v
Sodium polycarboxylate (Sopropon T36)	0.2% w/v
Attaclay (Attagel)	1.5% w/v

Antifoam (Rhodorsil AF426R)	0.003% w/v
Water	to 100 volumes

by stirring the above ingredients together and milling in a bead mill.

Example C4

A water dispersible granule is formed from:

Active ingredient (Compound 1)	50% w/w
Sodium dodecylbenzenesulphonate (Arylan SX 85)	3% w/w
Sodium methyl oleoyl taurate (Arkopon T)	5% w/w
Sodium polycarboxylate (Sopropon T36)	1% w/w
Binder (Sodium lignosulphonate)	8% w/w
China clay	30% w/w
Microfine silicon dioxide (Tixosil 38)	3% w/w

by blending the above ingredients together, grinding the mixture in an air jet mill and granulating by addition of water in a suitable granulation plant (e.g. Fluid bed drier) and drying. Optionally the active ingredient may be ground either on its own or admixed with some or all of the other ingredients.

The compounds of the invention have been used in herbicidal applications according to the following procedures.

METHOD OF USE OF HERBICIDAL COMPOUNDS:

TEST METHOD A

a) General

Appropriate quantities of the compounds used to treat the plants were dissolved in acetone to give solutions equivalent to application rates of up to 4000g test compound per hectare (g/ha). These solutions were applied from a standard laboratory herbicide sprayer delivering the equivalent of 290 litres of spray fluid per hectare.

b) Weed control : Pre-emergence

The seeds were sown in 70 mm square, 75 mm deep plastic pots in non-sterile soil . The quantities of seed per pot were as follows:-

Weed species	Approx number of seeds/pot
1) Broad-leafed weeds	
Abutilon theophrasti	10
Amaranthus retroflexus	20
Galium aparine	10
Ipomoea purpurea	10
Sinapis arvensis	15
Xanthium strumarium	2
2) Grass weeds	
Alopecurus myosuroides	15
Avena fatua	10
Echinochloa crus-galli	15
Setaria viridis	20
3) Sedges	
Cyperus esculentus	3

Crop	
1) Broad-leafed	
Cotton	3
Soya	3
2) Grass	
Maize	2
Rice	6
Wheat	6

The compounds of the invention were applied to the soil surface, containing the seeds, as described in (a). A single pot of each crop and each weed was allocated to each treatment, with unsprayed controls and controls sprayed with acetone alone.

After treatment the pots were placed on capillary matting kept in a glass house, and watered overhead . Visual assessment of crop damage was made 20-24 days after spraying. The results were expressed as the percentage reduction in growth or damage to the crop or weeds, in comparison with the plants in the control pots.

c) Weed control : Post-emergence

The weeds and crops were sown directly into John Innes potting compost in 75 mm deep, 70 mm square pots except for Amaranthus

which was pricked out at the seedling stage and transferred to the pots one week before spraying. The plants were then grown in the greenhouse until ready for spraying with the compounds used to treat the plants. The number of plants per pot were as follows :-

1) Broad leafed weeds

Weed species	Number of plants per pot	Growth stage
Abutilon theophrasti	3	1-2 leaves
Amaranthus retroflexus	4	1-2 leaves
Galium aparine	3	1st whorl
Ipomoea purpurea	3	1-2 leaves
Sinapis arvensis	4	2 leaves
Xanthium strumarium	1	2-3 leaves

2) Grass weeds

Weed species	Number of plants per pot	Growth stage
Alopecurus myosuroides	8-12	1-2 leaves
Avena fatua	12-18	1-2 leaves
Echinochloa crus-galli	4	2-3 leaves
Setaria viridis	15-25	1-2 leaves.

3) Sedges

Weed species	Number of plants per pot	Growth stage
Cyperus esculentus	3	3 leaves.

1) Broad leafed

Crops	Number of plants per pot	Growth stage
Cotton	2	1 leaf
Soya	2	2 leaves.

2) Grass

Crops	Number of plants per pot	Growth stage
Maize	2	2-3 leaves
Rice	4	2-3 leaves
Wheat	5	2-3 leaves.

The compounds used to treat the plants were applied to the plants as described in (a). A single pot of each crop and weed species was

allocated to each treatment, with unsprayed controls and controls sprayed with acetone alone.

After treatment the pots were placed on capillary matting in a glass house, and watered overhead once after 24 hours and then by controlled sub-irrigation. Visual assessment of crop damage and weed control was made 20-24 days after spraying. The results were expressed as the percentage reduction in growth or damage to the crop or weeds, in comparison with the plants in the control pots.

TEST METHOD B

Paddy post-emergence application in greenhouse

Paddy field soil was filled in 170 cm^2 plastic pots, a suitable amount of water and chemical fertilisers were added thereto and kneaded to convert it to a state of a paddy.

Paddy rice plants (variety; Koshihikari), that had been grown in advance in a greenhouse to a stage of two leaves, were transplanted to each pot (two seedlings per pot). Then in each pot there were sown predetermined amounts of seeds of Echinochloa oryzicola, Monochoria vaginalis, Lindernia procumbens and Scirpus juncoides respectively, and water was added to a depth of 3 cm.

After having grown the plants in a greenhouse until Echinochloa oryzicola reached a stage of 1.5 leaves, solutions were prepared in 100% acetone using compounds described in the Examples so that they contained active ingredients in an amount equivalent to 75, 300 and 1200 g/ha. The solutions were applied by dropping with a pipette.

After 21 days from the application with the chemicals, herbicidal effects on each weed and phytotoxicity on paddy rice plants were visually assessed, and the results expressed as the percentage reduction in growth or damage to the crop or weeds in comparison with the plants in the control pots.

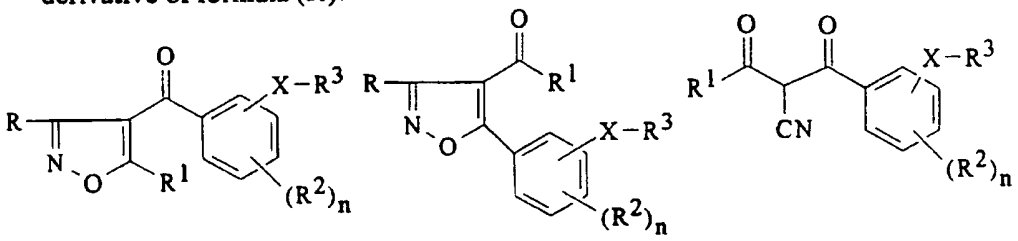
When applied pre- or post-emergence in Test Method A at 1000g/ha compounds 14-16, 26-29, 48, 73-76, 82, 127, 128, 136, 199, 200, 210, 211, 219, 263, 326-328, 331-338, 341, 342, 345-347, 349-351, 353, 354, 356, 359-363 and 369-371 gave at least 90% reduction in growth of one or more of the weed species; at levels of application toxic

to the weeds these compounds were selective in at least one of the crop species.

When applied at 1200 g/ha or less, in Test Method B, compounds 14, 15, 26, 27, 48, 73-76, 82, 127, 128, 199, 200, 210, 219, 262, 263, 326-335, 337-360 and 362-371 of the invention gave at least 90% reduction in growth of one or more of the weed species listed above.

CLAIMS

1. A 4-benzoylisoxazole derivative of formula (Ia), a 5-phenylisoxazole derivative of formula (Ib) or a 2-cyano-1,3-dione derivative of formula (Ic):



(Ia) (Ib) (Ic)

wherein:

R represents hydrogen or $-CO_2R^4$;

R^1 represents:-

a straight- or branched- chain alkyl group containing up to six carbon atoms which is optionally substituted by one or more halogen atoms; or

a cycloalkyl group containing from three to six carbon atoms optionally substituted by one or more R^{12} groups or one or more halogen atoms;

R^2 represents:-

halogen;

a straight- or branched- chain alkyl group containing up to six carbon atoms which is substituted by one or more groups $-OR^5$;

a cycloalkyl group containing from three to six carbon atoms; or a group selected from nitro, cyano, $-CO_2R^5$, $-S(O)_pR^7$, $-O(CH_2)_mOR^5$, $-COR^5$, $-NR^5R^6$, $-N(R^8)SO_2R^7$, $-OR^7$, -OH, $-OSO_2R^7$, $-(CR^9R^{10})_tS(O)_qR^7$, $-CONR^5R^6$, $-N(R^8)-C(Z)=Y$, $-C(R^9R^{10})NR^8R^{11}$ and R^{12};

or two groups R^2, together with adjacent carbon atoms of the phenyl ring, form a 1,3-benzodioxole ring which is optionally substituted by one or two halogen atoms at the 2-position of the 1,3-benzodioxole ring;

n represents zero or an integer from one to three; where n is greater than one the groups R^2 may be the same or different;

m represents one, two or three;

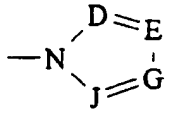
p represents zero, one or two;

q represents zero, one or two;

t represents one, two, three or four;

X represents $-C(R^{13}R^{14})-$; or $-C(R^{13a}R^{14a})-C(R^{15}R^{16})$;

R^3 represents a 5-membered heteroaromatic ring of formula (II)



(II)

in which D, E, G and J independently represent $-CR^{17}-$ or a nitrogen atom, with at least one of D, E, G and J representing a CR^{17} group;

two adjacent groups D, E, G and J may together form a second phenyl or 5- to 7- membered heteroaromatic ring optionally substituted by one or more groups R^{13b}, in which the 5- to 7- membered heterocyclic ring contains from one to four heteroatoms in the ring which may be the same or different selected from nitrogen, oxygen and sulphur;

R^4 represents:-

a straight- or branched- chain alkyl group containing up to six carbon atoms optionally substituted by one or more groups selected from halogen, $-OR^5$, $-CO_2R^5$, $-S(O)_pR^7$, phenyl and cyano;

or phenyl optionally substituted by one or more groups selected from halogen, $-OR^5$ and R^{12};

R^5 and R^6 which may be the same of different, each represents hydrogen or R^{12};

R^7 represents:-

R^{12}; or a cycloalkyl group containing from three to six carbon atoms; or a group $-(CH_2)_w$-[phenyl optionally substituted by from one to five groups R^{17a} which may be the same or different];

w represents zero or one;

R^8 represents:-

hydrogen;

a straight- or branched- chain alkyl, alkenyl or alkynyl group containing up to ten carbon atoms optionally substituted by one or more halogen atoms;

a cycloalkyl group containing from three to six carbon atoms;

$-(CH_2)_w$-[phenyl optionally substituted by from one to five groups R^{17a} which may be the same or different];

or $-OR^{18}$;

R^9 and R^{10} independently represent hydrogen or a straight- or branched- chain alkyl group containing up to six carbon atoms optionally substituted by one or more halogen atoms;

R^{11} represents $-S(O)_qR^7$ or -C(Z)=Y;

R^{12} represents:-

a straight- or branched- chain alkyl, alkenyl or alkynyl group containing up to six carbon atoms optionally substituted by one or more halogen atoms;

R^{13}, R^{13a}, R^{14a} and R^{15} independently represent R^5;

R^{13b} represents halogen or R^{12};

R^{14} represents R^5, cyano, $-OR^{12}$, $-S(O)_pR^{12}$ or halogen;

R^{16} represents R^5, cyano, $-OR^{12}$ or $-S(O)_pR^{12}$;

R^{17} represents:-

a group selected from hydrogen, halogen, R^{18}, nitro, cyano, $-CO_2R^5$, $-S(O)_pR^{18}$, $-OR^{18}$, $-NR^5R^6$ or cyclopropyl;

R^{17a} represents R^{17} with the exclusion of hydrogen and cyclopropyl;

R^{18} represents a straight- or branched- chain alkyl group containing up to six carbon atoms which is optionally substituted by one or more halogen atoms;

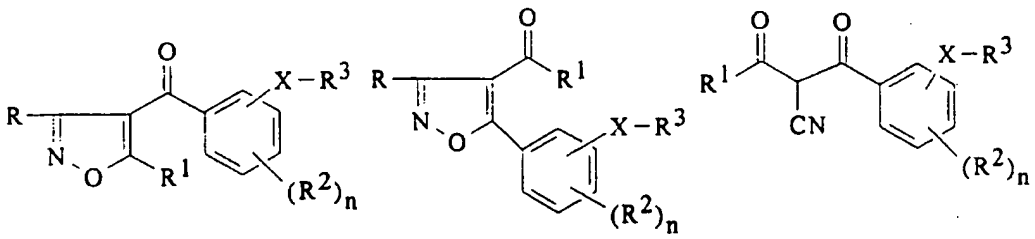
Y is oxygen or sulphur;

Z represents a group selected from R^{12}, $-NR^8R^{19}$, $-NR^8$-$NR^{19}R^{20}$, $-SR^7$ and $-OR^7$;

R^{19} and R^{20} independently represent R^8;

or an agriculturally acceptable salt or metal complex thereof.

2. A 4-benzoylisoxazole derivative of formula (Ia), a 5-phenylisoxazole derivative of formula (Ib) or a 2-cyano-1,3-dione derivative of formula (Ic):



(Ia) (Ib) (Ic)

in which R represents hydrogen or $-CO_2R^4$;

R^1 represents:-

a straight- or branched- chain alkyl group containing up to six carbon atoms which is optionally substituted by one or more halogen atoms; or

a cycloalkyl group containing from three to six carbon atoms optionally substituted by one or more R^{12} groups or one or more halogen atoms;

R^2 represents:-

halogen;

a straight- or branched- chain alkyl group containing up to six carbon atoms which is substituted by one or more groups $-OR^5$;

a cycloalkyl group containing from three to six carbon atoms; or a group selected from nitro, cyano, $-CO_2R^5$, $-S(O)_pR^7$, $-O(CH_2)_mOR^5$, $-COR^5$, $-NR^5R^6$, $-N(R^8)SO_2R^7$, $-OR^7$, -OH, $-OSO_2R^7$, $-(CR^9R^{10})_tSO_qR^7$, $-CONR^5R^6$, $-N(R^8)-C(Z)=Y$, $-C(R^9R^{10})NR^8R^{11}$ and R^{12};

or two groups R^2, together with adjacent carbon atoms of the phenyl ring, form a 1,3-benzodioxole ring which is optionally substituted by one or two halogen atoms at the 2-position of the 1,3-benzodioxole ring;

n represents zero or an integer from one to three; where n is greater than one the groups R^2 may be the same or different;

m represents one, two or three;

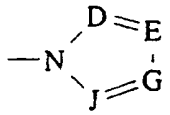
p represents zero, one or two;

q represents zero, one or two;

t represents one, two, three or four;

X represents $-C(R^{13}R^{14})-$; or $-C(R^{13a}R^{14a})-C(R^{15}R^{16})$;

R^3 represents a 5-membered heteroaromatic ring of formula (II)



(II)

in which D, E, G and J independently represent - CR^{17}- or a nitrogen atom, with at least one of D, E, G and J representing - CR^{17}-;

two adjacent groups D, E, G and J may together form a second phenyl or 5- to 7- membered heteroaromatic ring optionally substituted by one or more groups R^{13b}, in which the 5- to 7- membered heterocyclic ring contains from one to four heteroatoms in the ring which may be the same or different selected from nitrogen, oxygen and sulphur;

R^4 represents:-

a straight- or branched- chain alkyl group containing up to six carbon atoms optionally substituted by one or more groups selected from halogen, -OR^5, -CO_2R^5, -$S(O)_pR^7$, phenyl and cyano;

or phenyl optionally substituted by one or groups selected from halogen, -OR^5 and R^{12};

R^5 and R^6 which may be the same of different, each represents hydrogen or R^{12};

R^7 represents:-

R^{12}; or a cycloalkyl group containing from three to six carbon atoms; or a group -$(CH_2)_w$-[phenyl optionally substituted by from one to five groups R^{17a} which may be the same or different];

w represents zero or one;

R^8 represents:-

hydrogen;

a straight- or branched- chain alkyl, alkenyl or alkynyl group containing up to ten carbon atoms optionally substituted by one or more halogen atoms;

a cycloalkyl group containing from three to six carbon atoms;

-$(CH_2)_w$-[phenyl optionally substituted by from one to five groups R^{17a} which may be the same or different];

or -OR^{18};

R^9 and R^{10} independently represent hydrogen or a straight- or branched- chain alkyl group containing up to six carbon atoms optionally substituted by one or more halogen atoms;

R^{11} represents $-S(O)_qR^7$ or $-C(Z)=Y$;

R^{12} represents:-

a straight- or branched- chain alkyl, alkenyl or alkynyl group containing up to six carbon atoms optionally substituted by one or more halogen atoms;

R^{13}, R^{13a}, R^{14a} and R^{15} independently represent R^5;

R^{13b} represents halogen, or R^{13} with the exclusion of hydrogen;

R^{14} represents R^5, cyano, $-OR^{12}$, $-S(O)_pR^{12}$ or halogen;

R^{16} represents R^5, cyano, $-OR^{12}$ or $-S(O)_pR^{12}$;

R^{17} represents a group selected from hydrogen, halogen, R^{18}, nitro, cyano, $-CO_2R^5$, $-S(O)_pR^{18}$, $-OR^{18}$ and $-NR^5R^6$;

R^{17a} represents R^{17} with the exclusion of hydrogen;

R^{18} represents a straight- or branched- chain alkyl group containing up to six carbon atoms which is optionally substituted by one or more halogen atoms;

Y is oxygen or sulphur;

Z represents a group selected from R^{12}, $-NR^8R^{19}$, $-NR^8-NR^{19}R^{20}$, $-SR^7$ and $-OR^7$;

R^{19} and R^{20} independently represent R^8;

or an agriculturally acceptable salt or metal complex thereof.

3. A compound according to Claim 1 or 2 which is a compound of formula (Ia).

4. A compound according to Claim 1, 2 or 3 in which the 2-position of phenyl is substituted.

5. A compound according to Claim 1, 2, 3 or 4 in which the $-XR^3$ group is at the 2- or 3- position of phenyl.

6. A compound according to any one of the preceding Claims in which X represents $-CHR^{13}-$ and R^{13} is as defined in Claim 1 or 2.

7. A compound according to any one of the preceding Claims in which R^3 represents an N-linked ring of formula (II) in which:-

(a) D is nitrogen and E, G and J represent CR^{17};

(b) D, G and J are CR^{17} and E is nitrogen;

(c) D and G are nitrogen and E and J are CR^{17}; or

(d) D and E are nitrogen and G and J are CR^{17}.

8. A compound according to any one of the preceding Claims in which R^{17} is hydrogen, a straight- or branched- chain alkyl group containing up to six carbon atoms, $-S(O)_pR^{18}$ or cyclopropyl.

9. A compound according to any one of the preceding Claims in which the 5- and 6- positions of phenyl are unsubstituted.

10. A compound according to any one of the preceding Claims in which R^1 represents a straight- or branched- chain alkyl group containing up to three carbon atoms which is optionally substituted by one or more halogen atoms; or cyclopropyl or 1-methylcyclopropyl.

11. A compound according to any one of the preceding Claims in which R^2 represents halogen; a straight- or branched- chain alkyl or alkenyl group containing up to four carbon atoms optionally substituted by one or more halogen atoms; or a group selected from nitro, cyano, $-S(O)_pR^7$, $-OR^7$ and -OH.

12. A compound according to any one of the preceding Claims in which n represents zero, one or two.

13. A compound according to Claim 1 in which:

R represents hydrogen or a group $-CO_2R^4$;

R^1 represents cyclopropyl;

R^2 represents halogen; a straight- or branched- chain alkyl group containing up to three carbon atoms optionally substituted by one or more halogen atoms; or $-S(O)_pR^7$; or two groups R^2, together with adjacent carbon atoms of the phenyl ring, form a 1,3-benzodioxole ring which is optionally substituted by one or two halogen atoms at the 2-position of the 1,3-benzodioxole ring;

X represents $-CH_2-$, -CH(Me)- or -CH(Et)-;

R^3 represents a pyrazole, imidazole or 1,2,4-triazole ring optionally substituted on the ring carbon atoms by one or two groups selected from a straight- or branched- chain alkyl group containing up to four carbon atoms, $-S(O)_pR^{18}$ or cyclopropyl;

R^4 represents a methyl or ethyl group;

R^7 represents a methyl or ethyl group which is optionally substituted by one or more halogen atoms;

R^{18} represents methyl or ethyl; and

n and p represent 0, 1 or 2.

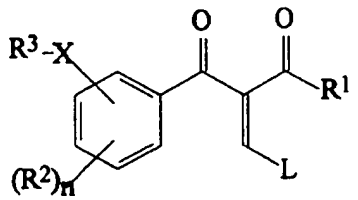
14. A compound of formula (Ia) as defined in Table 1.

15. A composition comprising a herbicidally effective amount of at least one compound of formula (Ia), (Ib) or (1c) as defined in any one of Claims 1 to 14, or an agriculturally acceptable salt or metal complex thereof, in association with an agriculturally acceptable diluent or carrier and/or surface-active agent.

16. A method for the control of the growth of weeds at a locus which comprises applying to the locus a herbicidally effective amount of at least one compound of formula (Ia), (Ib) or (1c) as defined in any one of Claims 1 to 14, or an agriculturally acceptable salt or metal complex thereof, or a composition according to Claim 15.

17. A process for preparing a compound of formula (Ia), (Ib) or (Ic) as defined in Claim 1 or 2 , the process comprising:

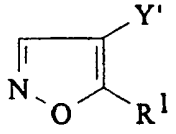
(a) where the compound is of formula (Ia) or (Ib) in which R represents hydrogen and R^1, R^2, R^3, X and n are as defined in Claim 1 or 2, reacting a compound of formula (IIa):



(IIa)

wherein L is a leaving group and R^1, R^2, R^3, n and X are as defined in Claim 1 or 2, with hydroxylamine or a salt of hydroxylamine;

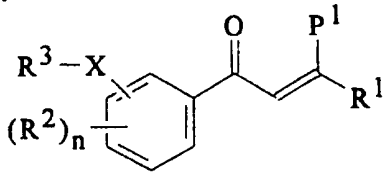
(b) where the compound is of formula (Ia) in which R represents hydrogen and R^1, R^2, R^3, X and n are as defined in Claim 1 or 2, reacting a compound of formula (III):



(III)

wherein R^1 is as defined in Claim 1 or 2 and Y' represents a carboxy group or a reactive derivative thereof or a cyano group, with an appropriate organometallic reagent;

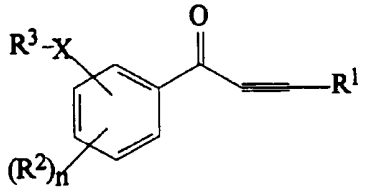
(c) where the compound is of formula (Ia) and R represents a group $-CO_2R^4$ and R^1, R^2, R^3, R^4, X and n are as above in Claim 1 or 2, reacting a compound of formula (IV):



(IV)

wherein R^1, R^2, R^3, X and n are as defined in Claim 1 or 2 and P^1 is a leaving group, with a compound of formula $R^4O_2CC(Z^1)$=NOH wherein R^4 is as defined in Claim 1 or 2 and Z^1 is as defined above;

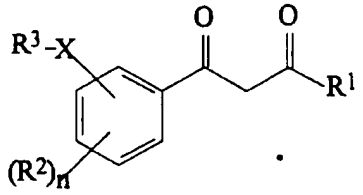
(d) where the compound is of formula (Ia) in which R represents a group $-CO_2R^4$ and R^1, R^2, R^3, R^4, X and n are as defined in Claim 1 or 2, reacting a compound of formula (V):



(V)

wherein R^1, R^2, R^3, X and n are as defined in Claim 1 or 2, with a compound of formula $R^4O_2CC(Z^1)$=NOH wherein R^4 is as defined in Claim 1 or 2 and Z^1 is as defined above;

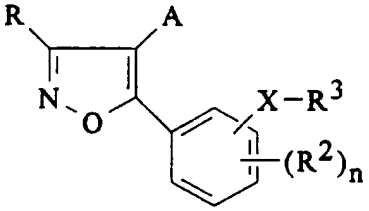
(e) where the compounds of formula (Ia) or (Ib) in which R represents $-CO_2R^4$ and R^1, R^2, R^3, R^4, X and n are as defined in Claim 1 or 2, reacting a salt of a compound of formula (VI):



(VI)

wherein R^1, R^2, R^3, X and n are as defined in Claim 1 or 2, with a compound of formula $R^4O_2CC(Z^1)$=NOH wherein R^4 is as defined in Claim 1 or 2 and Z^1 are as defined above;

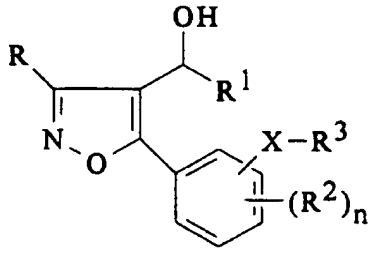
(f) where the compound is of formula (Ib) in which R, R^1, R^2, R^3, X and n are as defined in Claim 1 or 2, metallating a compound of formula (VII):



(VII)

wherein R, R^2, X and n are as defined in Claim 1 or 2 and A is a halogen atom, followed by reaction of the compound thus obtained with an acid chloride of general formula R^1COCl, wherein R^1 is as defined in Claim 1 or 2;

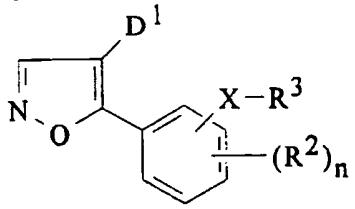
(g) where the compound is of formula (Ib) in which R, R^1, R^2, R^3, X and n are as above in Claim 1 or 2, oxidising a compound of formula (VIII):



(VIII)

to convert the hydroxy group to a ketone group;

(h) where the compound is of formula (Ib) in which R represents hydrogen and R^1, R^2, R^3, X and n are as defined in Claim 1 or 2, reacting a compound of formula (IX):



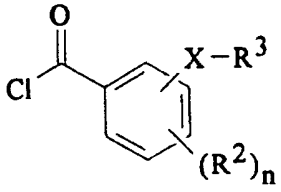
(IX)

in which D^1 represents a carboxy group, or a reactive derivative thereof (such as a carboxylic acid chloride or carboxylic ester), or a cyano group, with an appropriate organometallic reagent of formula R^1M^1 wherein R^1 is as defined in Claim 1 or 2 and M^1 is a metal halide or a metal;

(i) where the compounds is of formula (Ic), treating the corresponding compound of formula (Ia) or (Ib) in which R is hydrogen with a base;

(j) where the compounds is of formula (Ic), hydrolysing the corresponding compound of formula (Ia) or (Ib) in which R is $-CO_2R^4$ and R^4 is as defined in Claim 1 or 2, or in which R is replaced by an amide or nitrile;

(k) where the compounds is of formula (Ic), reacting a benzoyl chloride of formula (XIV):



(XIV)

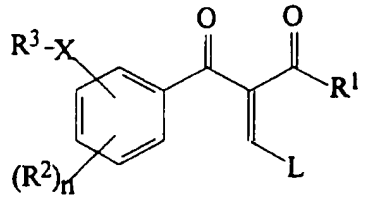
wherein R^2, R^3, X and n are as defined in Claim 1 or 2, with a beta-ketonitrile of formula (XV):

$$R^1C(=O)CH_2CN \qquad (XV)$$

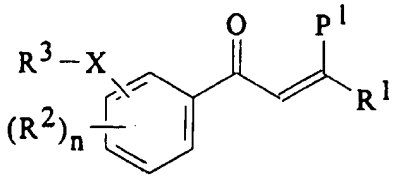
wherein R^1 is as hereinbefore defined in Claim 1 or 2;

optionally followed by the conversion of the compound thus obtained into an agriculturally acceptable salt or metal complex thereof.

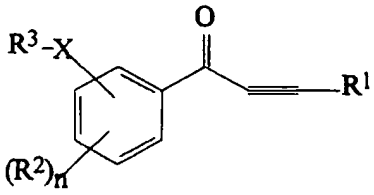
18. A compound of formula (IIa), (IV), (V), (VI), (VII), (VIII), (IX), (X), (XXX) or (XXXI):



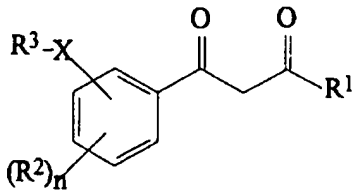
(IIa)



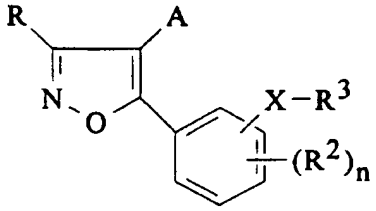
(IV)



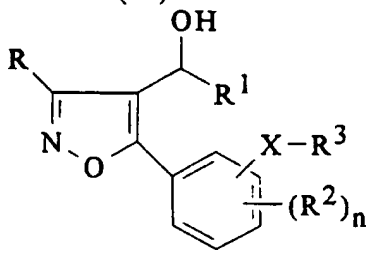
(V)



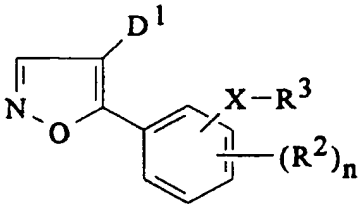
(VI)



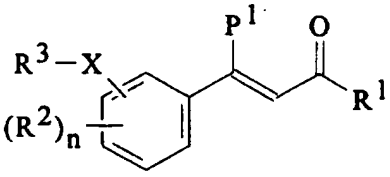
(VII)



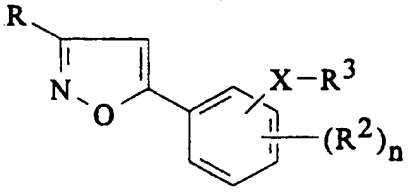
(VIII)



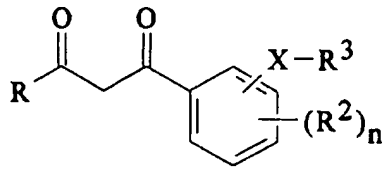
(IX)



(X)



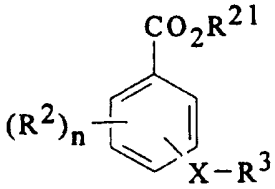
(XXX)



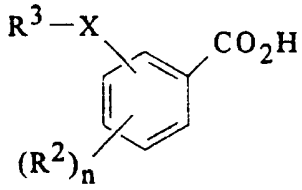
(XXXI)

wherein R^1, R^2, R^3, X and n are as defined in Claim 1 or 2, L is alkoxy or N,N-dialkylamino, A is halogen, and D^1 is carboxy or a reactive derivative thereof, or CN.

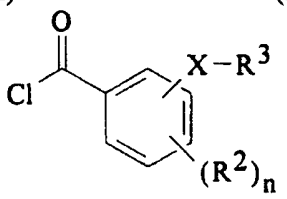
19. A compound of formula (XIV), (XXIII) or (XXV):



(XXIII)



(XXV)



(XIV)

wherein R^2, R^3, X and n are as defined in Claim 1 or 2 and R^{21} represents alkyl of from one to six carbon atoms.

INTERNATIONAL SEARCH REPORT

Inter ..al Application No
PCT/EP 97/00258

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C07D413/06 A01N43/80 C07D231/12 C07D249/08

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C07D C07C

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 0 625 505 A (RHONE POULENC AGRICULTURE LTD) 23 November 1994 see claims	1-16
A	EP 0 418 175 A (RHONE POULENC AGRICULTURE LTD) 20 March 1991 cited in the application see claims	1-16
A	EP 0 524 018 A (RHONE POULENC AGRICULTURE LTD) 20 January 1993 cited in the application see claims	1-16

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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"&" document member of the same patent family

1

Date of the actual completion of the international search	Date of mailing of the international search report
7 April 1997	14.04.97

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax (+31-70) 340-3016	Henry, J

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Information on patent family members

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information on patent family members

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